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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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EFFECTIVENESS OF COMBINED SURGICAL AND HORMONAL THERAPY IN TREATMENT OF ENDOMETRIOMAS

Chikhashvili E[1], Kristesashvili J[2], Urjumelashvili M[3].

[1]*MD, Phd. Student, Iv. Javakhishvili Tbilisi State University, Faculty of Medicine, Department of Clinical and Research Skills, Tbilisi, Georgia.*

[2]*Associated Professor of Iv. Javakhishvili Tbilisi State University, Faculty of Medicine, Department of Obstetrics – Gynecology – Reproductology, Tbilisi, Georgia.*

[3]*MD PHD, Assistant Professor, The Faculty of Medicine at University Geomedi, Georgia.*

Abstract.

Introduction: Endometrial cyst, or endometrioma, is a specific form of endometriosis that often reveals with severe symptoms and requires ongoing treatment. High rate of recurrence after surgical intervention presents a significant challenge in the management of this disease.

Aim of the study: Aim of the study was to determine the effectiveness of combined therapy (surgical and hormonal) of endometrioma in terms of development of recurrences, the rate of pregnancy and change in pain intensity.

Material and methods: Study group consisted of 264 patients with endometrioma who underwent laparoscopic intervention with enucleation of endometrial cyst. The study group was divided into: Group I - patients who were treated with dienogest for 6 months continuously (n-58); Group II - patients treated with combined contraceptives (COC) for 6 months cyclically (n-62); Group III - patients treated with dydrogesterone for 6 months, cyclically (n-45); Group IV - control group, patients who did not undergo postoperative hormone treatment (n-99).

Results: At 5-year post-operative follow-up, the pregnancy rate was significantly higher in Gr.I (72.4% (n-21), P<0.01) compared to control (34.8% (n-8)) and Gr.III (47.2% (n-17), P<0.05). No significant difference in terms of pregnancy occurrence was found between Gr.III and the control group (P>0.05). Assessment of pregnancy rate in Gr. II was not available as none in this group desired pregnancy. In Gr. I and Gr. III recurrence of endometrial cyst did not develop in any case, in Gr. II endometrioma recurrence was observed at 1.6%, which is significantly lower compared to control group (18.2%, P<0.01). No significant difference between the groups of hormone therapy was detected (P>0.05). After the hormone therapy, severe pain was not observed in any of the patients. Pain transformed from severe to moderate in Gr.I in 59.4% , in Gr. II – in 44.5% , in Gr. III – in 76.2%, in the control group -in 93.7% of cases and no longer experienced pain in Gr.I - 40.6%, in Gr.II -in 55.5%, in Gr.III – in 23.8%, in the control group – in 6.3 % . Treatment with dienogest and COC after surgery was found to be significantly more effective compared to the results obtained with Dydrogesterone (P<0.05) or surgical treatment alone (P<0.05). In patients with moderate pain, pain of moderate intensity did not remain in any patient in Gr.I, in Gr.II it remained at 3.8%, in Gr.III- in 16% and in the control group - in 46.9% (n-39). All forms of hormone therapy were found to be significantly more effective compared to treatment with surgical intervention alone (P<0.05). No significant difference was found between the methods of hormone therapy in terms of moderate pain intensity (P>0.05).

Conclusion: After surgical treatment of endometrioma, in cases of using different hormonal medications (Dienogest, COC, Dydrogesterone), the rate of recurrence of endometrioma is significantly lower compared to surgical intervention only, and the effectiveness of different hormonal medications showed no significant difference between groups.

Pregnancy rate is significantly higher in Dienogest and Dydrogesterone groups compared to only surgical intervention.

In cases of severe pain, treatment with Dienogest and COC is significantly effective compared with Dydrogesterone therapy or surgery alone. In cases of moderate pain all forms of hormone therapy were found to be significantly more effective compared to surgical intervention alone.

Key words. Endometrioma, recidives, dienogest, treatment of endometrioma.

Introduction.

Endometriosis is a chronic progressive gynecological disease characterized by the presence of the tissue similar to endometrium growing outside the uterus [1-4]. It occurs in about 10-15% of women of reproductive age and is characterised by chronic pelvic pain, dysmenorrhea, dyspareunia, and infertility [1,5,6].

Endometrioma often causes severe symptoms and requires continuous treatment, and high rate of recurrence after surgical intervention presents a significant challenge in the management of this disease. Determination and identification of risk factors for the formation and recurrence of endometrial cysts is of vital importance in the effectiveness of pre- and post-surgical treatment [7].

Inflammatory processes, hormonal imbalance, and immune system dysfunction are thought to contribute to the development of endometrial cysts [8]. Estrogens play an important role in the growth and development of endometriomas, which explains the effectiveness of hormone therapy in their treatment [9].

Endometrial cysts represent an important clinical problem for several reasons: pain syndrome, infertility, decreased ovarian reserve, risk of malignancy [10-15].

Currently, laparoscopy is considered as an approved and effective method of treatment of endometriomas due to its good tolerance, low risk of complications and acceptable cost [16,17]. However, the high probability of recurrence of endometrioma makes surgical treatment insufficiently effective [18].

Many studies have analyzed the recurrence rate of endometriomas after laparoscopic surgery, which occurs in 11-30% of cases during 2-year follow-up [5,18-22] and 10-50% in the first 5 years after surgery [23-29]. Thus, in patients with endometriomas, the combination of conservative and surgical

treatment is considered the most effective treatment tactic due to the low probability of recurrence and high rate of achieving pregnancy [30].

For more than 60 years, progestins have been used with great success for the treatment of endometriosis, but in some cases, this therapy is still ineffective. Effect of progestins on target cells appears to depend on the expression of progesterone receptors (PR), but PR expression is often impaired in endometrial areas, and therefore the effect of progestins on target cells is impaired. In case of prescribing combined hormonal contraceptives, in addition to the above, the possible negative effect of the estrogenic component on endometriotic areas is added [31,32]. It is noteworthy that by binding to progesterone receptors (PRs), progestins can induce anti-estrogenic, pro-apoptotic, anti-inflammatory and anti-neurogenic effects, which leads to the cessation of pain and pathogenetic mechanisms in endometrial lesions [33-36]. Thus, understanding of the mechanisms of therapeutic success and failure is essential for clinical decision-making [31].

Despite the above, surgical treatment of endometrial cysts remains the 'gold standard', especially for large (>3 cm) cysts [17,37]. Due to the high risk of recurrence, it has become important to develop an effective post-surgical drug treatment strategy in the management of endometrial cysts [38].

Many studies confirm the effectiveness of Dienogest in the prevention of recurrence of endometrial cysts [22,38-42]. In a 4-year study of 523 women by Y Ota, Kurashiki et al. in patients receiving Dienogest, endometrial cyst recurrence did not occur in any case. Recurrence occurred in 10% of cases in patients receiving COC, and in the control group recurrence occurred in 38% of cases [39]. Similar results were obtained in a 2019 study by Ouchi et al. [43]. A meta-analysis by Park et al. in 2019 compared Dienogest and GnRH agonists and found dienogest to be as effective in recurrence prevention with a better tolerability profile [3]. In a study by Yap et al., there was a statistically significant benefit of hormone therapy in the development of endometrial cyst recurrence, but no advantage was found in pain and pregnancy rates when hormone therapy was compared with surgery alone [40]. There are contradictive data in the literature that in patients who underwent post-operative hormonal therapy with different hormonal medications, endometrial cyst recurrence developed at a significantly higher rate compared to women who did not receive post-operative hormone therapy [19,20,21].

Impact of post-surgical treatment on endometrioma remains unclear. The inconsistency of literature data may be caused by the different duration of post-operative follow-up of patients and unspecified criteria for the definition of recurrence.

Dienogest is a fourth-generation progestin that has been developed specifically for the treatment of endometriosis [44,45]. Its unique pharmacological profile includes high progesterone activity on the endometrium, anti-androgenic activity and moderate anti-gonadotropic effect [42,45-48]. Dienogest acts against endometriosis by several mechanisms, namely, it causes atrophy of endometrial foci, reduces inflammatory processes, inhibits angiogenesis and increases apoptosis in endometrial cells [42,43,45,49,50]. It is important to note that Dienogest has minimal effects on bone mineral density, making it an advantage over GnRH agonists for long-term use [49,51-55].

As it is known, combined oral contraceptives contain a combination of estrogen and progestin. Their mechanism of action in the treatment of endometriosis includes suppression of ovulation, endometrial atrophy, reduction of prostaglandin production, and reduction of menstrual bleeding [56].

Many studies have also been conducted to determine the effectiveness of COCs in preventing the recurrence of endometrial cysts. A study by Cucinella et al. (2013) compared COCs and Dienogest. They found that both treatments were effective in preventing relapse, although Dienogest showed better results (recurrence rate 9.8% vs 13.7% after 2 years) [46].

Dydrogesterone is a synthetic progesterone that is structurally similar to endogenous progesterone [56,57]. Its mechanism of action includes stabilization of the endometrium, reduction of inflammatory processes and immunomodulatory effect [57]. It is important to note that Dydrogesterone does not have androgenic, estrogenic or glucocorticoid effects, which reduces the risk of side effects [56,57]. Effectiveness of dydrogesterone in preventing the recurrence of endometrial cysts is less studied compared to dienogest and COCs.

According to the studies available in the literature, Dienogest is most effective in preventing endometrial cyst recurrence [3,34,38,39,41,43,46,57]. COCs are also effective, although less than Dienogest [8].

A number of studies have been conducted to determine the effectiveness of different hormonal medications for the pain syndrome associated with endometriosis. According to some researchers, Dienogest and Dydrogesterone are relatively more effective in managing chronic pain than COC [56,58-61].

Vercellini et al. (2008) in a meta-analysis assessed the effectiveness of COCs in the treatment of pain associated with endometriosis and concluded that COCs significantly reduce pain and improve quality of life [4,62]. In 2007 Trivedi et al. conducted a randomized controlled trial comparing dydrogesterone and placebo in patients with endometriosis. They found that dydrogesterone significantly reduced symptoms and improved quality of life [14,56]. Similar results were obtained by Overton et al. and Tsai et al. [63,64]. In a 2017 study, dydrogesterone and Dienogest were compared. They concluded that both treatments were effective in reducing pain associated with endometriosis, although dienogest showed better results [61,64]. Thus, in the management of endometriosis, it is necessary to use individual approaches and make decisions based on the needs of patients.

Since the results of the research conducted in these areas are contradictory in some cases, the continuation of the research is relevant and appropriate.

Aim of the study.

Aim of the study was to determine the effectiveness of surgical and combined (surgical and hormone therapy) therapy in patients with endometrioma in terms of development of recurrences and the rate of pregnancy, as well as change in pain intensity.

Materials and Methods.

A retrospective observational research design was selected for the study. In order to conduct the study, approval N6 of the Ethical Commission of the “Zhordania Medical Clinic” was obtained. Before inclusion in the study, all patients participating

in the study were informed about the essence and aim of the study and written informed consent was obtained for inclusion in the study.

Inclusion criteria: Patients with histomorphologically established endometrioma after surgical intervention. **Exclusion criteria:** Patients with adenomyosis, patients with impaired hormonal background, patients who had taken any hormonal drugs for 6 months before surgery, patients who had underwent surgical intervention on the genitals, patients who had abnormalities of the development of genital organs, history of reproductive organ tumors, women with tubal factor infertility, male factor infertility.

Study group consisted of 264 patients with endometrioma who underwent laparoscopic intervention with enucleation of endometrial cyst in 2016-2022 yy. Barrier contraception was used in all patients for 3 months after the surgery. Patients included in the study were advised to conceive naturally after 3 months of using barrier contraception. Observation was made 5 years after the surgical intervention.

The study group was divided into the following groups:

Group I - patients who were treated after surgical treatment with Dienogest for 6 months continuously (n-58).

Group II - patients who were post-operatively treated with combined contraceptives (COC) for 6 months cyclically (n-62).

Group III - patients who were post-operatively treated with Dydrogesterone for 6 months, cyclically (n-45).

Group IV - control group, patients who did not undergo postoperative drug treatment (n-99).

In order to determine the recurrence all participants underwent an ultrasound examination of small pelvic organs on the 2nd–3rd days of the menstrual cycle. Ultrasound was performed with VOLUSON E10 (produced by General Electric, USA). Assessment of pain intensity was carried out before surgery and after surgery, in a period of 5 years, using a specially developed questionnaire.

Statistical analysis.

Statistical analysis was performed using descriptive and inferential methods. The research data was processed with statistical analysis program SPSS 24.0 (Statistical Package for Social Sciences, version 24). In order to describe the data, the percentage distribution of frequencies, standard deviation, crosstabulation, Kolmogorov-Smirnov test (to check the normality of the distribution) were used for quantitative variables. Categorical variables are presented as percentages. X2 test was used to determine the association between categorical variables. A statistically significant difference in the reduction of the mean intensity of dysmenorrhea and chronic pelvic pain in each study group, before and after laparoscopic intervention was determined by t test. Power 0.8, α-level numerical value was defined as 0.05, P value <0.05.

Results.

Out of 264 patients participating in the study, 88 patients wanted to get pregnant (see Table 1). Out of 88 women who wanted to get pregnant, pregnancy occurred in 46 cases (52,3 %) within 12 months after stopping hormone treatment (see Table 2). It should be noted that none of the patients who took COCs had the desire to become pregnant.

Table 1. *Desired pregnancy by groups.*

	Group I (n-58)	**Group II (n-62)**	**Group III (n-45)**	**Group IV (n-99)**
Desired pregnancy	50% (n-29)	0	80% (n-36)	23.2% (n-23)

Table 2. *Rate of achieved pregnancies according to groups in the period of 5 years after surgical intervention.*

	Group I (n-29)	**Group III (n-36)**	**Control group (n-23)**
Frequency of pregnancy	72.4% (n-21)	47.2% (n-17)	34.8% (n-8)
P	P<0.01 P¹<0.05	P>0.05	

P - Groups I and III vs control group
P¹ - Groups I vs III

As can be seen in Table 2, the rate of pregnancy was significantly higher in patients who received Dienogest post-operatively compared with control patients and also compared with patients who received Dydrogesterone. Between patients receiving Dydrogesterone and patients in the control group, there was no significant difference in the occurrence of pregnancy during the 5-year follow-up period.

In our study, we also assessed the rate of post-operative recurrence of endometriomas in women who received hormonal therapy (Dienogest, COC, Dydrogesterone) and compared with a control group, where no medication therapy was administered post-operatively. It was found that no recurrence developed after taking Dienogest and Dydrogesterone. After taking the COC, it was found only in 1 case (1,6%). The rate of recurrence in the control group was 18.2% (n-18), which is significantly higher than the indicators of each groups of hormone therapy, although no significant difference was detected between the groups of hormone therapy in terms of the development of recurrences (Table 3).

Table 3. *The rate of recurrence by groups after 5 years of surgery.*

Group	**Rate of recurrence**	**P**
Group I (n-58)	0	P<0.01 P¹>0.05 P²>0.05
Group II (n-62)	1,6 % (n -1)	P<0.01 P³>0.05
Group III (n-45)	0	P<0.05
Control group (n-99)	18,2% (n-18)	

P – Comparison of Groups I, II and III vs control group
P¹ – Comparison of Groups I vs Group II
P² - Comparison of Groups I vs III
P³ - Comparison of Groups II vs III

We also assessed pain intensity before surgery and compared it after hormone therapy in all four groups (Table 4).

In the study group (264 patients), severe pain was experienced by 78 patients (29.5%) before surgical treatment. Of these, the proportion of patients who received Dienogest after surgical treatment was 26.1% (n-32), COC - 14.5% (n-9), dydrogesterone - 45.7% (n-21), control group - 16.2% (n-16). After completion of the treatment, severe pain was not observed in any of the

Table 4. *Intensity of pain after completion of hormone therapy in patients with severe pain syndrome.*

Pain intensity	**Dienogest (n-32)**	**COC (n-9)**	**Dydrogesterone (n-21)**	**Control group (n-16)**
Severe	0	0	0	0
Moderate	59.4% (n-19)	44.5% (n-4)	76.2% (n-16)	93.7% (n-15)
No pain	40.6% (n-13)	55.5% (n-5)	23.8 (n-5)	6.3% (n-1)
P	P <0.05 P^1>0.05 P^2>0.05	P <0.05 P^3>0.05	P >0.05	

P – Comparison of Groups I, II and III vs control group
P^1 – Comparison of Groups I vs group II
P^2 - Comparison of Groups I vs group III
P^3 - Comparison of Groups II vs group III

Table 5. *Intensity of pain after completion of hormone therapy in patients with moderate pain syndrome.*

Pain intensity	**Dienogest (n-25)**	**COC (n-53)**	**Dydrogesterone (n-25)**	**Control group (n-83)**
Moderate	0	3.8% (n-2)	16% (n-4)	46.9% (n-39)
No pain	100% (n-25)	96.2% (n-51)	84% (n-21)	53.1% (n-44)
P	P <0.05 P^1>0.05 P^2>0.05	P <0.05 P^3>0.05	P <0.05	

P – Comparison of Groups I, II and III vs control group
P^1 – Comparison of Groups I vs II
P^2 - Comparison of Groups I vs III
P^3 - Comparison of Groups II vs III

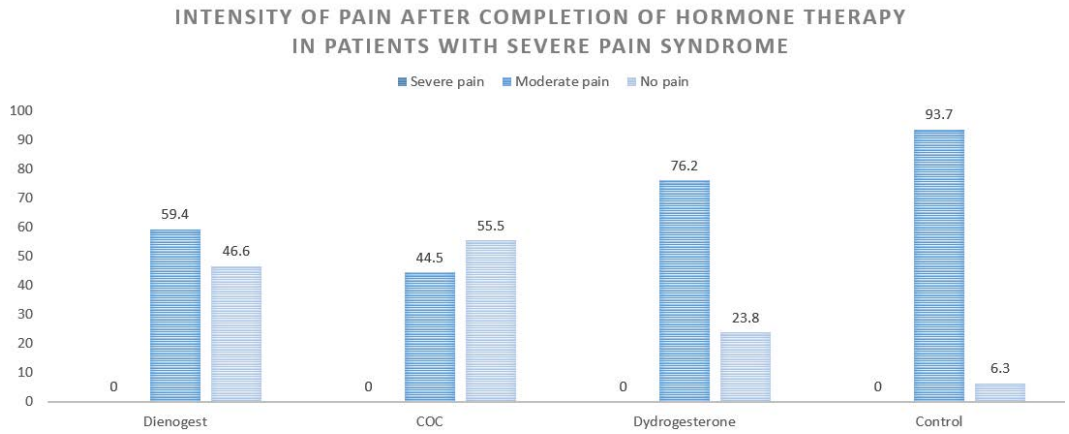

Figure 1. *Intensity of pain after completion of hormone therapy in patients with severe pain syndrome.*

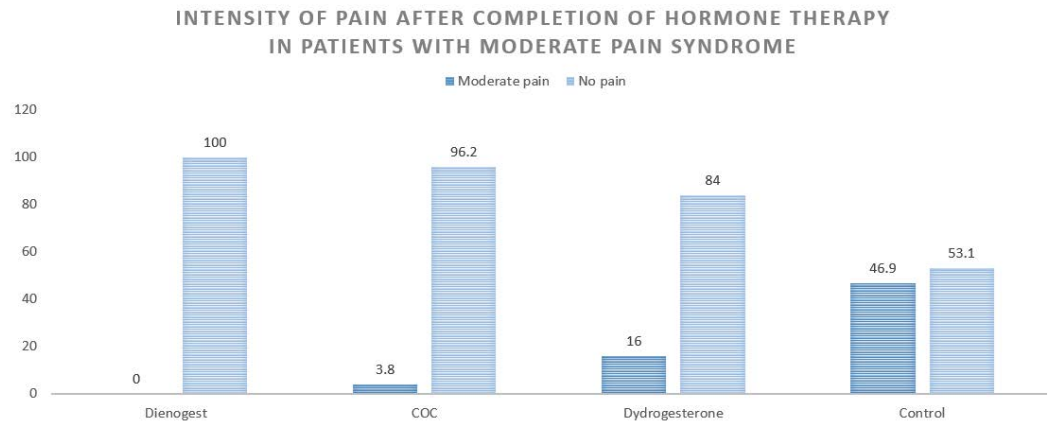

Figure 2. *Intensity of pain after completion of hormone therapy in patients with moderate pain syndrome.*

patients, the pain was alleviated in 59.4% of cases (n-19) in Gr. I, 44.5% (n-4) - in Gr.II, 76.2% (n-16) - in Gr. III, and 93.7% (n-16) in the control group (n-15), and no longer experienced pain in 40.6% of cases (n-13) in Gr. I, in Gr. II- 55.5% (n-5), in Gr. III - 23.8% (n-5), in the control group - 6.3 % (n-1). Treatment with Dienogest and COC after surgery was found to be significantly more effective than treatment with Dydrogesterone ($P<0.05$) or surgery alone ($P<0.05$). At the same time, no significant difference was found between the methods of hormone therapy in terms of pain intensity ($P>0.05$) (Table 4 and Figure 1).

In the study group (264 patients), moderate intensity pain was experienced by 186 patients (70.5%) before surgical treatment. Of these, the proportion of patients who received Dienogest after surgical treatment was 13.4% (n-25), COC - 28.5% (n-9), dydrogesterone - 13.4% (n-25), control group- 44.6% (n-83). After 6-months treatment course, pain was not observed in any of the patients of Gr. I, the moderate pain was maintained in 3.8% of cases (n-2) in Gr. II, 16% (n-4) - in Gr. III and 46.9% (n-39) in the control group. All forms of hormone therapy were found to be significantly more effective after surgery compared to treatment with surgical intervention alone ($P<0.05$). At the same time, no significant difference was found between the methods of hormone therapy in terms of pain intensity ($P>0.05$) (Table 5 and Figure 2).

Discussion.

Endometrioma is characterized with severe symptoms and requires ongoing treatment, and high rate of recurrence after surgical intervention presents a significant challenge in the management of this disease.

According to the data of our study, no recurrence developed after taking Dienogest and Dydrogesterone. After taking the COC, recurrence was found only in 1 case (1,6%). The rate of recurrence in the control group was 18.2% (n-18), which is significantly higher than the indicators of each group of hormone therapy. No significant difference was detected between each group of hormone therapy in terms of the development of recurrences of endometrioma.

There are data in the literature that in patients who underwent post-operative hormonal therapy with different hormonal medications, endometrial cyst recurrence developed at a significantly higher rate compared to women who did not receive post-operative hormone therapy [19,20,21]. These data contradict the data of our study and the data of a number of studies available in the literature [3,7,8,18-21,38,39,41,43,46].

According to data of our study, pregnancy occurred significantly more frequently in patients who received Dienogest postoperatively compared with control patients and also compared with patients who received Dydrogesterone. Between the patients who received Dydrogesterone and the patients of the control group, there was no significant difference in terms of pregnancy occurrence. However, a study by Yap et al. found no advantage in pregnancy rates with hormonal treatment compared with surgery alone [40].

In the study by Yap et al., they did not see an advantage in terms of reducing the intensity of pain in hormonal treatment compared to surgical treatment alone [40]. A number of studies show that post-operative use of dienogest significantly reduces pain and improves the quality of life of women [59,65,66], which is consistent with the data of our study, in particular, treatment with Dienogest and COC is significantly more effective in terms of pain intensity after surgery compared to treatment with Dydrogesterone or only surgery. Some studies suggest that the effectiveness of COCs, which contain both estrogen and progesterone, may be temporary and not sufficient to control pain [15,67-70]. According to other researchers, Dienogest and Dydrogesterone are relatively more effective in managing chronic pain than COC [58,59,70].

Therefore, it is necessary to use individual approaches and make decisions based on the needs of patients.

Conclusion.

After surgical treatment of endometrioma, in cases of using different hormonal medications (Dienogest, COC, Dydrogesterone), the rate of recurrence of endometrioma is significantly lower compared to surgical intervention only, and the effectiveness of different hormonal medications showed no significant difference between groups.

Pregnancy rate is significantly higher in Dienogest and Dydrogesterone groups compared to only surgical intervention.

In cases of severe pain, treatment with Dienogest and COC is significantly effective compared with Dydrogesterone therapy or surgery alone. In cases of moderate pain all forms of hormone therapy were found to be significantly more effective compared to surgical intervention alone.

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აბსტრაქტი
შესავალი: ენდომეტრიომა ხშირად იწვევს მძიმე სიმპტომებს და მოითხოვს მუდმივ მკურნალობას, ხოლო რეციდივების მაღალი მაჩვენებელი ქირურგიული ჩარევის შემდეგ, წარმოადგენს მნიშვნელოვან გამოწვევას ამ დაავადების მართვაში. კვლევის მიზანი: კვლევის მიზანს წარმოადგენდა ენდომეტრიომების კომბინირებული (ქირურგიული და ჰორმონული) თერაპიის ეფექტურობის დადგენა პაციენტებში ენდომეტრიომებით რეციდივების განვითარების, დაორსულების სიხშირის და ტკივილის ინტენსივობის ცვლილების თვალსაზრისით. მასალა და მეთოდები: საკვლევი ჯგუფი შეადგინა 264 პაციენტმა ენდომეტრიომით, რომელთაც ჩატარებული ჰქონდათ ლაპაროსკოპიული ჩარევა ენდომეტრიული ცისტის ენუკლეაციით. საკვლევი ჯგუფი დაიყო შემდეგ ჯგუფებად: I ჯგ. - პაციენტები, რომელთაც პოსტოპერაციულად ჩაუტარდათ მკურნალობა დიენოგესტით 6 თვის განმავლობაში უწყვეტად (n-58); II ჯგ.- პაციენტები, რომელთაც პოსტოპერაციულად ჩაუტარდათ მკურნალობა კოკ-ით 6 თვის განმავლობაში (n-62); III ჯგ.- პაციენტები, რომელთაც პოსტოპერაციულად ჩაუტარდათ მკურნალობა დიდროგესტერონით 6 თვის განმავლობაში ციკლურად (n-45); IVჯგ. - საკონტროლო ჯგუფი, პაციენტები, რომელთაც პოსტოპერაციულად არ ჩატარებიათ მედიკამენტოზური მკურნალობა (n-99). შედეგები: 5-წლიანი პოსტოპერაციული დაკვირვების

შემდეგ ორსულობის მაჩვენებელი მნიშვნელოვნად მაღალი იყო I ჯგუფში (72.4% (n-21), P<0.01) საკონტროლო (34.8% (n-8)) და III ჯგუფთან (47.2% (n-17) შედარებით, P<0.05). III და საკონტროლო ჯგუფს შორის დაორსულების სიხშირის თვალსაზრისით სარწმუნო სხვაობა არ გამოვლინდა (P>0.05). დაორსულების სიხშირის დადგენა II ჯგუფში ვერ მოხერხდა, რადგან ამ ჯგუფში არცერთს არ სურდა ორსულობა. I და III ჯგუფებში ენდომეტრიული ცისტის რეციდივი არცერთ შემთხვევაში არ განვითარდა, II ჯგუფში ენდომეტრიომის რეციდივი დაფიქსირდა 1.6%-ში, რაც სარწმუნოდ დაბალია საკონტროლო ჯგუფის მაჩვენებელთან შედარებით (18.2%, P<0.01). ჰორმონოთერაპიის ჯგუფების მონაცემებს შორის სარწმუნო სხვაობა არ გამოვლენილა (P>0.05). ჰორმონალური თერაპიის შემდეგ საკვლევი ჯგუფის არცერთ პაციენტს არ აღენიშნებოდა ძლიერი ტკივილი. საშუალო ინტენსივობის ტკივილი შეუნარჩუნდა I ჯგუფში 59.4%-ში, IIჯგ. – 44,5%-ში, III ჯგ. – 76.2%, საკონტროლო ჯგუფში - 93.7% შემთხვევაში. ტკივილი აღარ აღენიშნებოდა I ჯგუფში - 40.6%, II ჯგ. - 55.5%, III ჯგ - 23.8%, საკონტროლო ჯგუფში – 6.3%-ში. ქირურგიული ჩარევის შემდეგ დიენოგესტით და COC-ით მკურნალობა მნიშვნელოვნად უფრო ეფექტური აღმოჩნდა დიდროგესტერონის (P<0.05) ან მარტო ქირურგიული მკურნალობით მიღებულ შედეგებთან შედარებით (P<0.05). საშუალო ინტენსივობის ტკივილის მქონე პაციენტებიდან I ჯგუფში ტკივილი არცერთ პაციენტში არ აღენიშნა, II ჯგ-ში შენარჩუნდა 3.8%-ში, III ჯგ-ში - 16%-ში და საკონტროლო ჯგუფში - 46.9%-ში. აღმოჩნდა, რომ ჰორმონოთერაპიის ყველა ფორმა სარწმუნოდ უფრო ეფექტურია მხოლოდ ქირურგიულ მკურნალობასთან შედარებით (P<0.05). ტკივილის საშუალო ინტენსივობის თვალსაზრისით ჰორმონოთერაპიის მეთოდებს შორის სარწმუნო სხვაობა არ გამოვლინდა (P>0.05). დასკვნა: ენდომეტრიომის ქირურგიული მკურნალობის შემდეგ სხვადასხვა ჰორმონალური მედიკამენტების (დიენოგესტის, COC, დიდროგესტერონის) გამოყენების შემთხვევაში, ენდომეტრიომის რეციდივის სიხშირე მნიშვნელოვნად დაბალი იყო მხოლოდ ქირურგიულ ჩარევასთან შედარებით, ხოლო ჰორმონოთერაპიის ცალკეულ ჯგუფებს შორის სარწმუნო სხვაობა არ გამოვლინდა.

დაორსულების სიხშირე სარწმუნოდ მაღალი იყო დიენოგესტისა და დიდროგესტერონის ჯგუფებში მხოლოდ ქირურგიულ ჩარევასთან შედარებით.

ძლიერი ტკივილის შემთხვევაში, დიენოგესტით და COC-ით მკურნალობა სარწმუნოდ ეფექტურია დიდროგესტერონით თერაპიასთან ან მარტო ქირურგიულ მკირნალობასთან შედარებით. საშუალო ინტებსივობის ტკივილის შემთხვევაში ჰორმონოთერაპიის ყველა ფორმა მნიშვნელოვნად უფრო ეფექტური აღმოჩნდა მხოლოდ ქირურგიულ ჩარევასთან შედარებით.

Абстракт

Введение: Эндометриома часто сопровождается тяжелыми симптомами и требует постоянного лечения. Высокая частота рецидивов после хирургического вмешательства представляет собой серьезную дилемму в лечении этого заболевания.

Цель исследования: Целью исследования было определить эффективность комбинированного (хирургического и гормонального) лечения эндометриомы по показателям развития рецидивов, частоты наступления беременности и изменения интенсивности болевого синдрома.

Материалы и методы: Группу исследования составили 264 пациентки с эндометриомой, которым было выполнено лапароскопическое вмешательство с энуклеацией эндометриоидной кисты. Наблюдение осуществлялось в сроки до 5 лет после хирургического вмешательства. Группа исследования была разделена на следующие группы: I группа - пациентки, которым после хирургического вмешательства проводилась терапия диеногестом в течение 6 месяцев непрерывно (n-58); II группа - пациентки, которым после хирургического вмешательства проводилась терапия комбинированными контрацептивами (КОК) в течение 6 месяцев циклически по 21 дню с 5-го дня менструального цикла (n-62); III группа - пациентки, которым после хирургического вмешательства проводилась терапия дидрогестероном в течение 6 месяцев циклически по 10 дней с 16-го дня менструального цикла (n-45); IV группа - контрольная группа, пациентки, которым послеоперационное медикаментозное лечение не проводилось (n-99).

Результаты: Через 5 лет после операции частота наступления беременности была достоверно выше у пациенток, получавших диеногест после хирургического вмешательства (72,4% (n-21), P<0,01) по сравнению с контрольной группой (34,8% (n-8)), а также по сравнению с пациентками, получавшими дидрогестерон (47,2% (n-17), P<0,05). Достоверной разницы в частоте наступления беременности между пациентками, получавшими дидрогестерон, и пациентками контрольной группы не наблюдалось (P>0,05). После лечения диеногестом и дидрогестероном рецидив эндометриальной кисты не развился ни в одном случае, рецидив после применения КОК наблюдался только в 1 случае (1,6%), а частота рецидивов в контрольной группе составила 18,2% (n-18), P<0,01, что достоверно выше по сравнению с пациентками, получавшими гормональную терапию в каждой из групп. При этом не было выявлено достоверных различий между группами гормональной терапии по частоте рецидивов (P>0,05). После завершения гормональной терапии у пациенток не наблюдалось сильной боли. Боль средней интенсивности сохранялась в группе, получавшей диеногест, в 59,4% случаев (n-19), в группе, получавшей КОК — 44,5% (n-4), в группе, получавшей Дюфастон — 76,2% (n-16), в контрольной группе — 93,7% (n-15). Лечение диеногестом и КОК после операции оказалось достоверно более эффективным по сравнению с результатами, полученными при применении дидрогестерона (P<0,05) или только хирургическом лечении (P<0,05). После завершения

гормональной терапии боли средней интенсивности не оставались у никого из пациенток в группе диеногеста, в 3,8% (n-2) случаев — в группе, получавшей КОК, в 16% (n-4) случаев — у пациенток, получавших Дюфастон, и в контрольной группе — в 46,9% (n-39) случаев. Все формы гормональной терапии оказались значительно более эффективными после операции по сравнению с лечением только хирургическим вмешательством ($P<0,05$). При этом не было выявлено достоверных различий между методами гормональной терапии по интенсивности боли ($P>0,05$).

Выводы: После хирургического лечения эндометриомы при использовании различных гормональных препаратов (Диеногеста, КОК, Дидрогестерона), частота рецидивов эндометриомы достоверно ниже по сравнению с только хирургическим вмешательством, а эффективность различных гормональных препаратов не показала достоверной разницы между группами.

Частота наступления беременности достоверно выше в группах Диеногеста и Дидрогестерона по сравнению с только хирургическим вмешательством.

В случаях сильной боли лечение Диеногестом и КОК достоверно эффективнее по сравнению с терапией Дидрогестероном или только хирургическим вмешательством. В случаях умеренной боли все формы гормональной терапии оказались значительно эффективнее по сравнению с только хирургическим вмешательством.