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### Реферати

#### ПЕРИНАТАЛЬНІ НАСЛІДКИ ПОРУШЕННЯ АДАПТАЦІЇ ПРИ ОБТЯЖЕНОМУ АКУШЕРСЬКОМУ АНАМНЕЗІ

Жданович О.І., Воробей Л.І., Аношина Т.М., Коломійченко Т.В.

Пережитий стрес на тлі перинатальних втрат (ПВ) може негативно впливати на перебіг наступної вагітності. Проведено дослідження варіабельності серцевого ритму плода шляхом кардіоінтервалографії (КИГ) плода жінок з обтяженим акушерським анамнезом (ПВ в анамнезі) у 32-34 тижні вагітності. Обстежено 200 вагітних з ПВ та 100 вагітних без ПВ в анамнезі. Порівняння результатів кардіотокографії та доплерометрії з даними КИГ плода показало, що при зриві адаптації регуляторних систем плода його дистрес діагностовано у 90,0 % жінок, при вираженому напруженні регуляторних систем плода – у 27,3 %, тобто результати КИГ плода після 32 тижнів вагітності можуть бути діагностичними маркерами його дистресу. Переважна більшість (76,1 %) дітей від матерів з ПВ в анамнезі після перенесеного внутрішньоутробно дистресу народжуються у стані асфіксії, що обумовлює високу частоту синдромів дизадаптації, найчастішими з яких порушення ЦНС (73,9 %) та дизадаптації серцево-судинної системи (41,3 %).

**Ключові слова:** перинатальні втрати, кардіоінтервалографія, адаптація, дистрес плода, новонароджений

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#### ПЕРИНАТАЛЬНІ НАСЛІДКИ ПОРУШЕННЯ АДАПТАЦІЇ ПРИ ОБТЯЖЕНОМУ АКУШЕРСЬКОМУ АНАМНЕЗІ

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Пережитый стресс на фоне перинатальных потерь (ПП) может негативно влиять на течение последующих беременностей. Проведено исследование вариабельности сердечного ритма (ВСР) плода путем кардиоинтервалографии (КИГ) плода женщин с обтяженным акушерским анамнезом (ПВ в анамнезе) в 32-34 недели беременности. Обследованы 200 беременных с ПП и 100 беременных без ПП в анамнезе. Сравнение результатов кардиотокографии и доплерометрии с данными КИГ плода показало, что при срыве адаптации регуляторных систем плода его дистрес диагностирован у 90,0% женщин, при выраженном напряжении регуляторных систем плода - у 27,3%, то есть результаты КИГ плода после 32 недель беременности могут быть диагностическими маркерами его дистресса. Подавляющее большинство (76,1%) детей от матерей с ПП в анамнезе после перенесенного внутриутробно дистресс рождаются в состоянии асфиксии, обуславливает высокую частоту синдромов дизадаптации, частыми из которых нарушения ЦНС (73,9%) и дизадаптації серцево-судинної системи (41,3%).

**Ключевые слова:** перинатальные потери, кардиоинтервалография, адаптация, дистрес плода, новорожденный

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#### PREVENTION OF PURULENT-SEPTIC COMPLICATIONS DURING LAPAROSCOPIC SURGERIES ON PELVIC ORGANS WITH THE RISK OF VAGINAL MICROBIOTA CONTAMINATION

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The efficacy analysis of the purulent-septic complications prevention at 115 "clean-contaminated" laparoscopic surgeries on the pelvic organs (laparoscopic hysterectomy, conservative myomectomy with the node resection via colpotomy incision) was performed. In the experimental group of patients (n = 60), 0.02% decamethoxin solution was administered intravaginally. The control group (n = 55) received traditional systemic perioperative antibiotic prevention using cephalosporins. It was shown that the early postoperative period dynamics, as well as indicators of systemic inflammatory response and the number of complications did not show significant differences between the studied groups, and in the experimental group there was an increase in the lactobacilli number and 87.3% decrease in the opportunistic pathogens content, which indicated the feasibility of preventive intraoperative topical decamethoxin application.

**Key words:** laparoscopy, purulent-septic complications, prevention, decamethoxin.

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Endoscopic surgery has a clear place in modern surgical gynecology. Due to the minimal invasiveness, high precision and operative endoscopic technique improvement, the incidence of postoperative purulent-septic complications (PSC) in endoscopic gynecological operations does not exceed 3.5% and depends on the complexity, surgery duration, the presence of risk factors, including vaginal microbiota contamination [1].

Most gynecological surgeries performed by laparoscopic approach are "clean-contaminated", requiring the prophylactic administration of antibacterial drugs in order to counterbalance the benefits of this minimally invasive surgical method [1-3, 5]. The drug choice for the infectious-inflammatory complications prevention should be based on its clinical and pharmacoeconomic efficacy, taking into account the increased opportunistic pathogens virulence and the spread of antibiotic resistance [6, 8, 10]. The emergence of antibiotic-resistant microflora and the widespread of pan-resistant microorganisms significantly reduce the effectiveness of antibacterial prevention and increase the purulent-septic complications incidence [1, 4, 8].

Despite improving knowledge about pathogenesis of early purulent-septic complications and therapeutic technologies development, PSC incidence does not tend to decrease, especially in patients with extragenital and combined gynecological pathology, obesity, impaired neuroendocrine regulation, immune suppression, which often develops against the background of the frequent and uncontrolled application of antibacterial drugs [4, 9].

The results of numerous clinical studies on the application of antibacterial agents in the PSC prevention are quite controversial [7-9]. Difficulties in vaginal microbiome correction are usually attributed to the formation of biofilms by opportunistic pathogens, which matrix prevent the proper penetration of systemic antibacterial drugs and leads to increased resistance of microorganisms to antibiotics [1, 6, 10].

Therefore, it is important to find a rational way to prevent infectious complications in "clean-contaminated" surgeries on the pelvic organs with the risk of vaginal microbiota contamination.

**The purpose** of the study was to evaluate the effectiveness of topical application of decamethoxin for the purulent-septic complications prevention in "clean-contaminated" laparoscopic operations on the pelvic organs with the risk of the vaginal microbiota contamination.

**Materials and methods.** The study was performed at the Clinical Trial Centre of the Department of Obstetrics and Gynecology No. 1 at the Multidisciplinary Medical Center of Odesa National Medical University for the period of January 2017 to March 2019. 115 women with low risk of PSC, who underwent "clean-contaminated" laparoscopic surgeries (laparoscopic hysterectomy, myomectomy with wide opening of the posterior vaginal vault) were examined. The exclusion criteria were: intraperitoneal bleeding, presence of urogenital infections, acute or chronic pelvic inflammatory diseases, systemic diseases (diabetes, immunodeficiency, obesity), allergic diseases, the history of laparotomy surgeries.

Depending on the method of antimicrobial prevention of PSC, patients were randomly assigned to two groups by random sampling. Experimental group (Group 1, n = 60) included patients who underwent surgery without systemic perioperative antibiotic prophylaxis (ABP), but with topical use of a disinfectant; the control group (Group 2, n = 55) included patients who underwent systemic perioperative ABP according to the traditional scheme (cephalosporins of II-III generation for 1 g intravenously with the beginning of anesthesia and again 1 g intravenously after 6-12 hours).

30 minutes before surgery, patients of the Group 1 were given intravaginally a swab, irrigated with 40.0-55.0 ml of 0.02% antiseptic solution, the active substance of which is decamethylenedimethylmethoxycarbonylmethylammonium dichloride (decamethoxin). Decamethoxin is a broad-spectrum antiseptic agent with bactericidal, fungicidal, virucidal and sporicidal activity, which has vaginal dysbiosis correction properties, contributes to the destruction of the bacterial biofilm matrix. Removal of this swab was performed during the emptying uterus or myomatous node from the abdominal cavity through the colpotomy incision.

To determine the degree of exo- and endogenous intoxication, a leukocyte index of intoxication (LII), which is an indicator of acute-phase inflammatory reactions according to Ya.Ya. Kalf-Kalif in the modification of B.A. Reys [6] was used.

The study of vaginal biotope before and after surgery included bacterioscopic and bacteriological studies [6, 8, 10]. In bacterioscopic examination, the preparations were stained by the Gram-Syniov, Romanovsky-Giemsa method, methylene blue, and microscopic at immersion; bacterial forms of microbiota were identified by the Berge method. The analysis of the vaginal bacterial spectrum and the recording of results were carried out in accordance with the Order of the Ministry of Health of Ukraine No. 234 of 2007. The number of bacteria in 1.0 ml of secretions was determined by the number of colonies that grew with the degree of the inoculum dilution.  $10^4$ - $10^5$  CFU/ml indicators were evaluated as the average degree of microbial genital contamination, at  $10^6$  or more – as a high degree [4, 10].

Laparoscopic surgery was performed according to the standard procedure under general endotracheal anesthesia, using special sets of equipment and instruments produced by "Karl Storz".

The study was performed in accordance with the ethical principles of the Helsinki Declaration on Bioethics and obtaining the written consent of patients to participate in the study.

Statistical processing of the results was performed using Microsoft Excel 2019.

**Results of the study and their discussion.** A study of 115 women aged 20-55 found that patients in both groups had complaints of abdominal or lumbar pain – 86 (74.8%) menstrual disorders – 57 (49.8%), weakness – 43 (37.4%), increased fatigue – 37 (32.2%), sexual disorders – 10 (8.7%). In 33 (28.7%) women, iron deficiency anemia of the first degree of severity was detected. There were no significant differences between the study groups (table 1).

Table 1

**Clinical characteristics of patients in the examined groups**

Clinical symptoms	In general	Group 1	Group 2	P
Abdominal or lumbar pain	86 (74.8%)	44 (73.3%)	42 (76.4%)	0.375
Menstrual disorders	57 (49.6%)	28 (46.7%)	29 (52.7%)	0.234
Overall weakness	43 (37.4%)	23 (38.3%)	20 (36.4%)	0.453
Increased fatigue	37 (32.2%)	18 (30%)	19 (34.5%)	0.305
Sexual Function Disorders	10 (8.7%)	4 (6.7%)	6 (10.9%)	0.197
Iron deficiency anemia of the first degree of severity	33 (28.7%)	16 (26.7%)	17 (30.9%)	0.316

Prevention of PSC in postoperative patients consisted of pre-operative, intra-and post-operative measures. Preoperative measures included a meticulous clinical and laboratory examination to exclude risk factors for postoperative inflammatory complications (subcompensated extragenital pathology, subclinical inflammatory processes, examination for sexually transmitted infections), and the vagina rehabilitation 3-5 days before surgery. Intraoperative PSC prevention consisted of the surgery technique with scrupulous hemostasis, minimal electrocoagulation, limited suture application, application of synthetic absorbable filaments, antibiotic prophylaxis before the anesthesia administration and again after 6-12 hours, drainage of the pelvic cavity.

Indicators of Complete Blood Count before surgery had no significant differences: hemoglobin level in the Group 1 was equal to  $120.2 \pm 0.1$  g/l, in the Group 2 –  $121.1 \pm 11.1$  g/l, White Blood Cell content was, respectively, in the Group 1  $7.9 \pm 0.5 \cdot 10^9/l$ , in the Group 2 –  $8.10 \pm 0.4 \cdot 10^9/l$ . Prior to surgery, mild leukocytosis and ESR increasing were noted in 17 (14.8%) cases, and LII before surgery was within the normal range in both study groups.

The study of the bacterial spectrum of the vagina in the examined patients showed that 44 (38.3%) had biotope disorders. Along with lactobacilli that have antimicrobial activity against opportunistic pathogens, associations of opportunistic microorganisms have been found in clinically significant concentrations. Most often, *E. coli*, *Enterococcus faecalis*, *Candida albicans*, *Bacillus*, *Corynebacterium* spp., *Staphylococcus aureus*, *Klebsiella* were sown.

The vaginal biotope state before surgery had no significant differences: I degree of vagina cleanliness was diagnosed in 61.7% of patients in Group 1 and in 61.8% in Group 2 ( $p = 1$ ), II degree of vagina cleanliness, respectively, in 38.6 and 37.9% of patients (Fisher's exact test  $p = 1$ ). Therefore, in examined patients were found endogenous ways of infection: the presence of a significant content of opportunistic bacteria and their associations.

All surgeries were planned and performed by laparoscopic approach: laparoscopic hysterectomy – in 67 (58.3%) patients, conservative myomectomy with posterior colpotomy – in 48 (41.7%) patients.

The duration of surgeries in both groups of patients did not differ ( $p=0.962$ ): in the experimental group it was  $79.5 \pm 19.1$  minutes, in the control group –  $80.5 \pm 7.4$  minutes. The mean volume of intraoperative blood loss in both groups was not significantly different and amounted to  $130.5 \pm 40.5$  ml.

Post-operative measures consisted of early motor activity of patients, physical therapy, monitoring of heart rate, body temperature, diuresis, as well as the LII monitoring, which characterizes the inflammation severity of cellular and plasma origin and is important for treatment monitoring and prognosis for the PSC development.

The vaginal biotope state before surgery had no significant differences: I degree of vagina cleanliness was diagnosed in 61.7% of patients in Group 1 and in 61.8% in Group 2 ( $p = 1$ ), II degree of vagina cleanliness, respectively, in 38.6 and 37.9% of patients (Fisher's exact test  $p = 1$ ).

In the postoperative period, an average hemoglobin content in the patients of both groups also did not differ; in both groups there was mild leukocytosis and ESR increasing; but in patients of Group 1 LII was within the normal range of  $1.20 \pm 0.02$  units, and in the Group 2 it was increased to  $1.80 \pm 0.04$  units (table 2).

In the study of vaginal biotope in the post-surgery period, in the Group 1 was found an increase in lactobacilli number and a decrease of 87.3% in the opportunistic microflora number (Fig. 1). Thus, the pathogenic flora number in the experimental group of patients decreased from  $5.1 \pm 0.1$  lg10 (CFU/ml) to  $3.4 \pm 0.1$  lg10 (CFU/ml), or by 87.3% ( $p < 0.001$ ), while in Group 2, this indicator had no significant changes (table 2).

Dynamics of clinical and laboratory parameters in the examined patients

Indices	Group 1 (Experimental, n=60)		Group 2 (Control, n=55)	
	Before treatment	After treatment	Before treatment	After treatment
White blood cells *10 <sup>9</sup> /l	7.9±0.5	9.2±0.5	8.1±0.4	9.3±0.3
LII, units	1.50±0.05	1.20±0.02*	1.50±0.05	1.80±0.04*
Number of opportunistic bacteria, lg10 (CFU/ml)	5.1±0.1	3.4±0.1*	5.1±0.1	4.9±0.1

Note: \* difference between pre- and post-surgery values, p <0.001

In the control group, lactobacilli decreased in 27 (49.1%) patients in the vaginal biotope and in 17 (30.9%) the Candida fungi growth was observed, which indicated dysbiotic disorders.

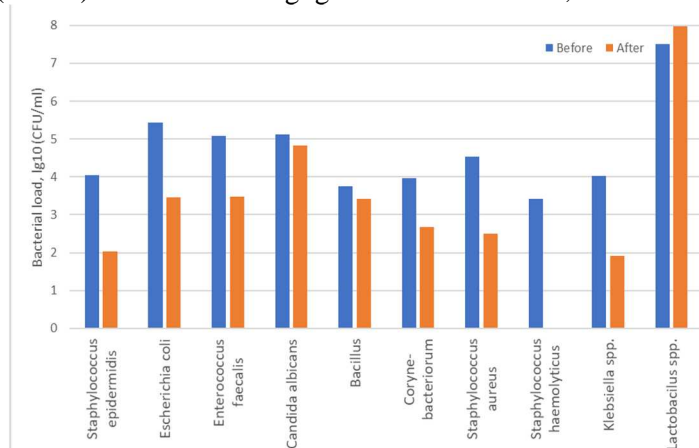


Fig. 1. Changes in vaginal biotope after antiseptic administration in the experimental group.

As a result of antiseptic administration for complex PSC prevention in patients of the experimental group in "clean-contaminated" laparoscopic surgeries in the postoperative period, LII decreased from 1.50±0.05 units to 1.20±0.02 units, and in the vaginal biotope significantly decreased the content of opportunistic microflora (p <0.01); while in the control group the LII indicator had a significant increase from 1.50±0.05 units to 1.80±0.04 units (p <0.01) and there were noted manifestations of dysbiosis (table 2).

The duration of the anesthesia period was 3.4±1.3 days versus 3.5±1.5 days, the period of intestinal function recovery was 3.5±1.5 days versus 2.4±0.9 days and the mean hospital stay of 3.0±0.4 days versus 3.2±0.3 days had no significant differences in the compared groups (table 3).

Table 3

Features of the post-surgery period course

Indices	Group 1	Group 2	p
Duration of anesthesia period, days	3.4±1.3	3.5±1.5	0.960
Intestinal function recovery, days	3.5±1.5	2.4±0.9	0.934
Post-surgery bed day, days	3.0±0.4	3.2±0.3	0.690

In the analysis of early postoperative complications, the PSC incidence was similar in both groups (table 4). There were no severe complications (subphrenic abscess, subhepatic abscess, pelvic cavity abscesses, intestinal abscesses, peritonitis).

In our opinion, the absence of severe forms of infectious-inflammatory complications in the examined groups is associated with careful patients selection without significant risk factors for PSC development (metabolic and endocrine disorders, urogenital infections, immunodeficiency states, allergic reactions, severe anemia, bleeding).

Table 4

Frequency of postoperative complications in studied groups

Indices	Group 1	Group 2	p
Fever >37.5 °C for more than 3 days	1 (1.7%)	1 (1.8 %)	0.496
Periculitis, inflammatory infiltrate of a colpotomy wound	1 (1.7%)	1 (1.8 %)	0.496
Signs of intestinal dysbiosis	1 (1.7%)	3 (5.5%)	0.131

The data obtained correlate with the results of studies by Ierano C. et al. (2017), which have shown that topical application of antiseptic agents for high-risk wounds causes a reduction in the infectious complications incidence [9]. Antibiotic prophylaxis should not be used as a temporary measure in the absence of timely application of antiseptics. Proper preoperative preparation and risk assessment are critical to preventing purulent-septic complications in the surgical site [6, 9].

Thus, the effectiveness of topical application of decamethoxin antiseptic solution, as well as the absence of negative factors inherent in systemic antibiotic prophylaxis (increase in the treatment cost, the risk of side effects; the risk of developing polyresistant bacterial strains; difficulty in diagnosis, the clinical picture "vague" of infectious complication), allows to recommend this method for optimization of PSC prevention at "clean-contaminated" laparoscopic surgeries on the pelvic organs with the risk of vaginal microbiota contamination.

**Conclusion**

The study showed that intravaginal application of decamethoxin in "clean-contaminated" gynecological surgeries contributes to the vaginal microbiome correction, 87.3% reduction in the content of opportunistic flora and the inflammatory processes intensity at the postoperative stage of treatment. The proposed method of treatment is effective and comparable to traditional antibiotic prophylaxis of complications (subject to careful selection of patients, adherence to scrupulous surgical technique and minimization of tissue injury).

*Prospects for further research* are to study the long-term results of treatment, as well as the cost-effectiveness of the proposed method of prevention of infectious-inflammatory complications in operations on the pelvic organs.

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**Реферати**

**ПРОФИЛАКТИКА ГНІЙНО-СЕПТИЧНИХ  
УСКЛАДНЕНЬ ПРИ ЛАПАРОСКОПІЧНИХ  
ОПЕРАЦІЯХ НА ОРГАНАХ МАЛОГО ТАЗА  
З РИЗИКОМ КОНТАМІНАЦІЇ ВАГІНАЛЬНОЇ  
МІКРОБІОТИ**

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Проведений аналіз ефективності профілактики гнійно-септичних ускладнень при 115 "умовно чистих" лапароскопічних операціях на органах малого таза (лапароскопічна гістеректомія, консервативна міомектомія з видаленням вузла через кольпотомний розтин). В основній групі хворих (n = 60) інтравагінально застосували 0,02 % розчин декаметоксину. Контрольна група (n = 55) одержувала традиційну системну периопераційну антибіотикопротекцію з використанням цефалоспоринів. Показано, що як за динамікою перебігу раннього післяопераційного періоду, так і показниками системної запальної відповіді і кількістю ускладнень достовірних відмінностей між досліджуваними групами не було. В основній групі мало місце збільшення кількості лактобацил і зменшення на 87,3% вмісту умовно-патогенної мікрофлори, що свідчило про доцільність профілактичного інтраопераційного місцевого застосування декаметоксину.

**Ключові слова:** лапароскопія, гнійно-септичні ускладнення, профілактика, декаметоксин.

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**ПРОФИЛАКТИКА ГНОЙНО-СЕПТИЧЕСКИХ  
ОСЛОЖНЕНИЙ ПРИ ЛАПАРОСКОПИЧЕСКИХ  
ОПЕРАЦИЯХ НА ОРГАНАХ МАЛОГО ТАЗА  
С РИСКОМ КОНТАМИНАЦИИ ВАГИНАЛЬНОЙ  
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Проведен анализ эффективности профилактики гнойно-септических осложнений при 115 "условно чистых" лапароскопических операциях на органах малого таза (лапароскопическая гистерэктомия, консервативная миомектомия с удалением узла через кольпотомный разрез). В основной группе больных (n = 60) интравагинально применяли 0,02% раствор декаметоксина. Контрольная группа (n = 55) получала традиционную системную периоперационную антибиотикопрофилактику с использованием цефалоспоринов. Показано, что как по динамике течения раннего послеоперационного периода, так и по показателями системного воспалительного ответа и количеством осложнений достоверных различий между исследуемыми группами не было. В основной группе имело место снижение степени эндогенной интоксикации, уменьшение на 87,3% содержания условно-патогенной микрофлоры, нормализация микробиоценоза, что свидетельствовало о целесообразности профилактического интраоперационного местного применения декаметоксина.

**Ключевые слова:** лапароскопия, гнойно-септические осложнения, профилактика, декаметоксин.

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