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Realities Of Time. Chronic Gender Inflammation And Pelvic Pain

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Abstract. ***One of the most pressing problems in modern gynecology is the problem of chronic inflammation of the appendages. Every obstetrician-gynecologist has to deal with a complaint of pain in the lower abdomen in women every day. About 39% of women experience pelvic pain caused by inflammation of the uterine appendages periodically, while 12% of patients experience pain for at least 5 days every month, and another 12% suffer from persistent pelvic pain [2]. Chronic pelvic pain occupies a special place among the variety of clinical manifestations of gynecological diseases and is considered by most researchers as one of the leading symptoms of inflammatory diseases of the pelvic organs: chronic salpingitis and oophoritis, pelvic peritoneal adhesions, chronic endometritis. However, the presence of a "routine" gynecological pathology cannot always explain the development of pain in the lower pelvis. Pelvic pain is an indication in 12% of all hysterectomies. For this reason, the aim of our study was to optimize the treatment of chronic inflammatory diseases of the uterine appendages to improve the quality of life and prevention of pelvic pain. The object of the study was 100 women with chronic salpingoophoritis complicated by pelvic pain, who were divided into three groups according to the method of treatment. During the study, we used, along with general clinical research methods and examination for sexually transmitted infections, special research methods, such as: studying the intensity of pain on the VAS scale, bacterioscopic and bacteriological examination of vaginal contents, ultrasound scanning and Doppler studies, estradiol, progesterone, testosterone, FSH, LH, DHEAS-S, TSH, prolactin and cortisol in the blood serum, the content of prostaglandins F2α, E2 and growth factors in the serum. In addition, the level of immunoglobulin A (IgA), the concentration of the main cytokines (IL 1β, IL6) in the blood serum were determined. The resulting material was subjected to automated statistical processing. After the examination, the patients received the necessary treatment, which included antibiotic-anti-inflammatory therapy (ceftriaxone, doxycycline, metronidazole), 20 procedures of pharmaco-physiotherapeutic intravaginal electrotherapy with the drug Glutoxim in an amount of 1 ml of 1% solution, intravaginal ultrasound therapy, synbiotic Bifiten. Based on the results of the data, the effectiveness of the use of the developed pharmaco-physiotherapeutic method (91%) was proved in comparison with intravaginal ultrasound therapy (74%) and, especially, drug therapy (40%).***

Keywords: chronic inflammation of the uterine appendages, pelvic pain, intravaginal electrotherapy, chronic salpingoophoritis, hysterectomy.

1. INTRODUCTION

Many authors who have studied the problem of complications of chronic inflammation note that chronic pelvic pain with CVPM is much more often a symptom of gynecological diseases (73.1%), but it also occurs with extragenital diseases (21.9%) and mental disorders (1.1%) [4]. Chronic pelvic pain occupies a special place among the variety of clinical manifestations of gynecological diseases and is considered by most researchers as one of the leading symptoms of inflammatory diseases of the pelvic organs: chronic salpingitis and oophoritis, pelvic peritoneal adhesions, chronic endometritis. Among the inflammatory diseases of the female genital organs, chronic forms of salpingoophoritis, accompanied by chronic pelvic pain, occupy one of the leading places and, according to various authors, account for 40.5-85% [1,7,12, 15]. The significance of the problem of salpingoophoritis is also due to the relatively frequent occurrence against its background of various forms of menstrual dysfunction, pathological reactions of the endocrine, nervous, immune and other body systems that carry out the response of the patient's body to the development of inflammation [9,11,17]. It is noted that they lead to irreversible functional and morphological disorders of the female reproductive system, and in 15.8% of cases to tubal infertility [8,11,13,16], causing profound dysfunctions of the associated organs and systems, which worsens the quality of life of women. Long-term existence of pain syndrome leads to a decrease in working capacity and the development of neuroses [5,19]. In this regard, chronic pelvic pain remains one of the most pressing problems in modern gynecology.

Achievements of modern medicine provide for the use of this pathology and the complications arising from it, both highly effective antibacterial and anti-inflammatory drugs, and the use of physiotherapeutic methods of therapy [6,8,16]. Despite this, the management of patient data is still not a fully resolved problem. In this regard, innovative methods of treatment of chronic salpingo-oopharitis, accompanied by chronic pelvic pain, involving the use of safe and natural physical factors, as well as pharmacotherapeutic methods of therapy, determine the relevance of the study of this problem.

2. MATERIALS AND THE METHODS OF RESEARCH:

Research work on the diagnosis and treatment of patients with chronic salpingo-oophoritis complicated by pelvic pain was carried out on the basis of the SamMI Clinic No. 1 in 100 patients of reproductive age (Table 1). The average age was 29.5 ± 2.1 years.

Table 1

Patient age	***%***
20 to 25 years old	**18**
25 to 30 years old	**29**
30 to 35 years old	**37**
35 to 40 years old	**35**
40 to 45 years old	**19**
Total	**100**

The duration of the disease in the patients was from 1 to 10 years with the duration of the pain syndrome from 1 to 7 years (on average, 2.3 ± 0.2 years).

For a comparative analysis, all women were divided into 3 subgroups comparable in terms of clinical and functional characteristics, depending on the method of treatment used:

- the main group - 35 patients who received a course of intravaginal electrotherapy;
- comparison group 1 - 35 patients who received a course of intravaginal ultrasound therapy;
- comparison group 2 - 30 patients who received local drug anti-inflammatory therapy, supporting fortifying and vitamin therapy, which was the background in the main group and in the 1st comparison group.

The criteria for the inclusion of women in the main group was the presence of pain in the region below the navel, above and medial to the inguinal ligaments, behind the womb and in the lumbosacral region, which bothered the patients for 6 months.

The study used general clinical research methods (general blood and urine analysis, ECG, R-graphical examination of the chest) and examination for sexually transmitted infections, as well as special research methods, including:

- the study of the intensity of pain syndrome according to the VAS scale consisted in the fact that the patients were asked to mark a point on a non-graduated line 10 cm long, which corresponds to the severity of pain;
- to analyze the state of the microbiocenosis, a bacterioscopic and bacteriological examination of the vaginal contents was carried out;
- ultrasound scanning and Doppler studies were performed on Mindray DC 4000 devices. Ultrasound was performed using convex and transvaginal transducers with a frequency of 3.5-5 MHz in the first phase of the menstrual cycle. Doppler studies were performed using vaginal transducers with the patients supine position, on days 3-6 of the menstrual cycle. The studies were carried out mainly in the afternoon (from 14:00 to 19:00);
- assessment of the hormonal status of women in the study groups was studied by determining the level in the blood serum of the concentration of estradiol, progesterone, testosterone, FSH, LH, DHEAS-S, TSH, prolactin and cortisol in the early follicular, periovulatory and luteal phases of the menstrual cycle. The studies were carried out using the Mindray MR 96A immunochemical system based on the methodenzyme immunoassay using XEMA reagent kits.

Determination of the content of prostaglandins F2α, E2 and growth factors in the blood serum was carried out by the method of enzyme immunoassay using RD&S reagent kits (Great Britain).

To determine the content of adrenaline, norepinephrine and serotonin, a competitive ELISA was performed using reagent kits from IBL (Germany).

The humoral link of immunity was studied by determining the level of immunoglobulin A (IgA), as well as the concentration of the main cytokines (IL 1β, IL6) in the blood serum using the Mindray MR 96A enzyme-linked immunosorbent assay with DAI (USA) and Diaclone (France) reagent kits. The studies were carried out before the start and 3 months after the end of treatment.

All the obtained material was subjected to automated statistical processing. The variational-statistical processing of the research results was carried out using the Statistic 6.0 software with the determination of the main variational indicators (mean values (M), mean errors (m), standard deviation (p)). The reliability of the results obtained was determined using the Student's test. Differences between the two mean values were considered significant if the p-parameter was less than 0.05. The reliability level was at least 95%.

Treatment methods included the following:

Drug antibacterial, anti-inflammatory, detoxification therapy included drugs recommended by the protocol:

- Ceftriaxone 250mg intramuscularly in a single dose;
- Doxycycline 100 mg IV or orally twice a day for 14 days;
- Metronidazole 500 mg orally twice a day for 14 days.

Pharmaco-physiotherapeutic intravaginal electrotherapy was performed on a BTL-4000 Premium G apparatus using a galvanic direct current. The exposure time was 20 minutes, daily, 2 times a day. The intensity was determined by the sensations of a pronounced but painless vibration under the flat electrode, maximum 12 mA. 20 procedures were performed. The drug Glutoxim was used as a drug in an amount of 1 ml of a 1% solution - an immunomodulator with a systemic cytoprotective effect, which is a promising agent in the treatment of chronic salpingo-oophoritis as an immunorehabilitation drug.
Intravaginal ultrasound therapy was performed on the BTL-4000 Premium G device with the following parameters: frequency of ultrasonic vibrations 0.88 MHz, effective emitter area 1 cm2, pulsed mode, intensity of ultrasonic vibrations 0.4 W / cm3, pulse duration 10 ms, pulse repetition rate 50 Hz, exposure time 8-10 minutes, daily for 10 days. For the procedures, a special vaginal ultrasound emitter was used, on which a condom was put on before the procedure and 5 ml of Repak gel was applied evenly on its surface (to create a full-fledged contact medium necessary for ultrasound) and the projection area of the uterine appendages was sonicated. After the procedure, the emitter was disinfected.
In addition, the synbiotic Bifiten was used, manufactured using the innovative technology MURE (Multi Resistant Encapsulation), which, in terms of qualitative and quantitative composition, meets all the requirements that should ensure the effectiveness and safety of complex preparations.
Evaluation of the effectiveness of therapy methods was carried out 14 and 30 days after the start of therapy.
Treatment regimens for patients of different groups are presented in Table 2.

Table 2

Treatment regimens for patients of different groups with chronic salpingoophoritis complicated by chronic pain

Group	**Preparations and methods**	**Dose**	**The course of therapy**
Basic	intravaginal electrotherapy with Glutoxim	1 ml of 1% solution	for 10 days, 2 times a day
	Bifiten	1 capsule	1 time per day for 10 days
	Primary therapy (ceftriaxone, metronidazole ,doxycycline)	By protocol	
1comparison group	Ultrasound therapy	10 days	
	Bifiten	1 capsule	1 time per day for 10 days
	Basic therapy	By protocol	

2comparison group	Ceftriaxone	250mg	intramuscularly in a single dose
	Metronidazole	500 mg	orally twice a day for 14 days
	Doxycycline	100 mg	orally twice a day for 14 days

3. RESULTS AND DISCUSSION

When studying complaints and anamnesis, along with pain syndrome, 50% of patients had a subfebrile temperature (up to 37.2 ° C), in 70% of cases there were complaints of vaginal discharge, in 75% of cases - a violation of the menstrual cycle, in 40% of cases - on frequent urination and in 22% of cases there was a violation of the act of defecation, which can be associated with the involvement of the associated organs in the adhesive process (Fig. 1).

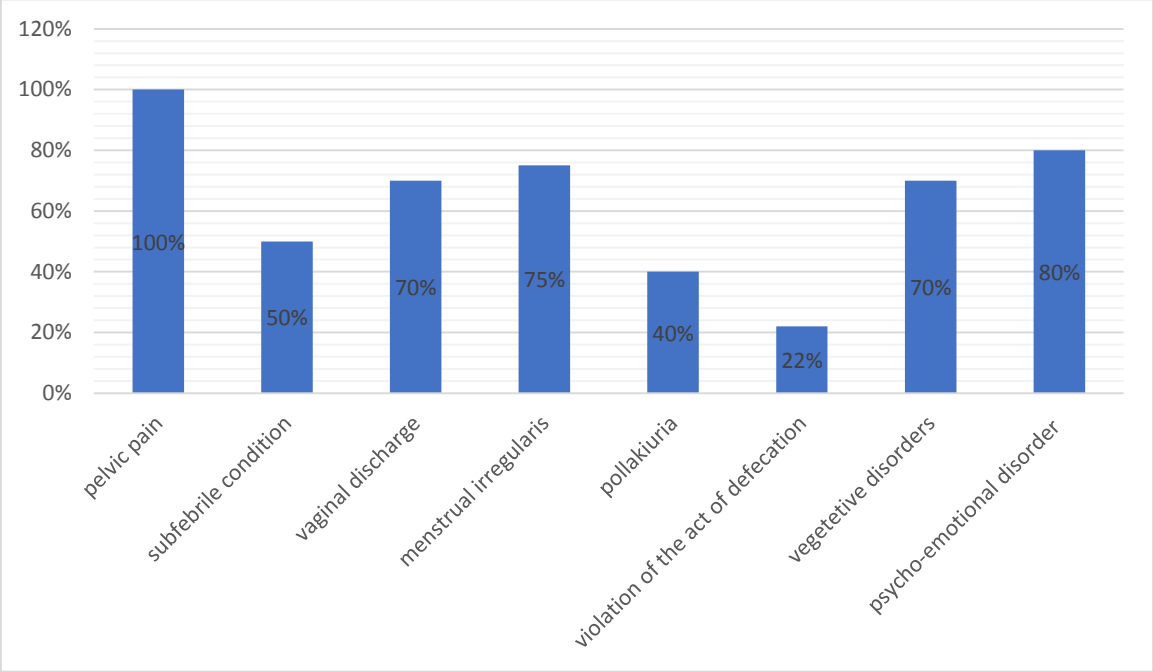

Figure: 1. Distribution of patients with chronic salpingoophoritis complicated by pelvic pain, depending on the presence of the main clinical manifestations of the disease,% Vegetative disorders were observed in 70% of cases, psychoemotional disorders were revealed in 80% of cases, which confirms the subjective manifestations of the disease characteristic of chronic salpingoophoritis.

Preliminary ultrasound examination confirmed the presence of a pronounced inflammatory process in the uterine appendages in women of all studied groups. In the patients included in the study, with transvaginal ultrasound, the presence of hyperplastic and hormone-dependent formations was excluded. In the overwhelming majority of patients, areas with increased echo density with uneven, indistinct contours in the uterine appendages were detected, which indicated the presence of an adhesive process. When studying the uterus, changes in the structure of the myometrium and endometrium were observed in 60% of patients. Have In most women, the ultrasound picture of the uterine appendages was characterized by a significant increase in their size both in longitudinal and transverse scanning against the

background of changes in their structure in the form of hyperechogenicity or alternating hyperechoicity with finely dispersed echo-negative inclusions. This may indicate the presence of small cysts.

A sign of chronic salpingoophoritis in 80% of cases was also the presence of a small amount of free fluid in the back of the uterine space.

Thus, during ultrasound, data were obtained that indicated functional disorders of an inflammatory nature in the region of the uterine appendages, as well as their structural disorders and the presence of an adhesive process, which is the result of chronic inflammation with frequent exacerbations.

During the analysis of the results of the influence of various methods of treating patients with chronic salpingoophoritis with the presence of chronic pain on the ultrasound picture, he confirmed the rather high anti-inflammatory effect of the pharmaco-physiotherapeutic method, manifested by an improvement in the shape and structure of the uterine appendages, as evidenced by a significant decrease in the areas of hyperechogenicity and the number of fine echo-negative inclusions in 91.4% of patients, which was significantly more significant than in the two comparison groups (74.3% and 60%, respectively). A decrease in the size of the ovaries to the indicators of healthy individuals was noted in 74.3% of patients in the main group, in the 1st comparison group, similar dynamics was also noted, but to a lesser extent, in the patients of the 2nd comparison group, there was a tendency to improve the ultrasound picture, but in a than in the first two degree groups.

Taking into account the important role of immune disorders in the pathogenesis of chronic salpingoophoritis, which directly affects the occurrence of chronic pain, we studied the most informative indicators of humoral immunity in this regard (Table 3).

Table 3

Dynamics of serum immunoglobulin parameters in patients with chronic salpingo-oophoritis complicated by pelvic pain under the influence of various treatment methods (M ± m)

Group			Main (n = 35) (M1 ± m)	Comparison 1 (n = 35) (M2 ± m)	Comparison 2 (n = 30) (M3 ± m)
Indicator	Norm	Before treatment	After treatment		
Ig A	0.6-4.5 g / l, 1.82 ± 0.04	4.8 ± 0.12 P1 ***	1.95 ± 0.05 P1 *, P2 ***	2.9 ± 0.17 P1 **, P2 *, P3 **	3.2 ± 0.14 P1 ***, P3 *
Ig M	0.6-3.7 g / l, 1.24 ± 0.02	2.4 ± 0.08 P1 ***	1.25 ± 0.06 P1 *, P2 ***	1.8 ± 0.09 P1 **, P2 **, P3 *	2.0 ± 0.07 P1 ***, P3 ***
Ig G	7.00-16.00 g / l, 10.5 ± 1.1	32.4 ± 2.5 P1 ***	11.7 ± 0.5 P2 ***	18.5 ± 0.8 P1 ***, P2 *, P3 ***	28.5 ± 0.6 P1 ***, P3 **

*Note: * - p <0.05; ** - p <0.01; *** - p <0.001, P1 - comparison with the norm, P2 - comparison with the parameters before treatment, P3 - comparison with the main group.*

Evaluating the humoral immunity in patients of all groups according to the parameters of serum immunoglobulins A, M, G, an increase in their values was found 2.6 times, 1.9 times and 3.1 times, respectively, which undoubtedly indicates a pronounced inflammatory process. After the course of therapy, we revealed statistically significant changes in serum immunoglobulin parameters. Thus, in the patients of the main group, a decrease in the values of serum immunoglobulins A, M, G by 2.5 times, 1.92 times and 2.8 times, respectively, was found in comparison with the indicators before treatment. Patients of the 1st comparison group showed a decrease in the values of serum immunoglobulins A, M, G by 1.6 times, 1.3 times and 1.7 times, respectively, compared with the indicators before treatment. Patients of the 2nd group of comparison showed a decrease in the values of serum immunoglobulins A, M, G by 1.5 times, 1.2 times and 1.1 times, respectively, in comparison with the indicators before treatment.

The study of the functional state of the hypothalamic-pituitary-ovarian system in women of the studied groups was carried out by determining the concentration of the main steroid hormones. When studying the hormonal background in the observed patients before treatment, endocrine disorders were noted both at the level of central and at the level of peripheral hormonal structures (Table 4).

Table 4

Dynamics of the hormonal status of patients with chronic salpingoophoritis complicated by pelvic pain under the influence of various treatment methods

(M ± m)

Group			Main (n = 35) (M1 ± m)	Comparison 1 (n = 35) (M2 ± m)	Comparison 2 (n = 30) (M3 ± m)
Hormone	Norm	Before treatment	After treatment		
Estradiol, pg / ml	58-480, 215.8 ± 6.2	65.7 ± 3.3 P1 ***	223 ± 6.4 P2 ***	169.4 ± 5.9 P1 *, P2 *	96.6 ± 3.2 P1 ***, P2 *, P3 ***
FSH, mIU / ml	1.7-25.0, 10.3 ± 0.5	27.12 ± 2.3 P1 ***	12.6 ± 0.05 P2 ***	18.4 ± 1.2 P1 *, P2 *	20.1 ± 2.5 P1 ***, P2 *, P3 ***
LH, luteal phase mIU / L	0.05 - 14.7, 5.6 ± 0.2	0.31 ± 0.02 P1 ***	5.7 ± 0.2 P2 ***	3.2 ± 0.15 P1 *, P2 *	0.74 ± 0.04 P1 ***, P2 *, P3 ***
Prolactin, follicular phase μIU / ml	136 - 999, 428.5 ± 19.3	942.12 ± 41.2 P1 ***	412.3 ± 18.7 P2 ***	538.6 ± 37.8 P1 *, P2 *	624.5 ± 41.3 P1 ***, P2 *, P3 ***
Cortisol, μg / dL	3.7 - 19.4, 14.8 ± 1.3	49.5 ± 3.8 P1 ***	15.5 ± 1.5 P2 ***	37.2 ± 2.1 P1 *, P2 *	47.4 ± 2.7 P1 ***, P2 *, P3 ***
Progesterone, luteal phase, ng / ml	2.2-17.9, 15.4 ± 1.7	1.2 ± 0.3 P1 ***	14.8 ± 1.3 P2 ***	9.5 ± 0.7 P1 *, P2 *	3.6 ± 0.3 P1 ***, P2 *, P3 ***

*Note: * - p <0.05; ** - p <0.01; *** - p <0.001; P1 - comparison with the norm, P2 - comparison with the parameters before treatment, P3 - comparison with the main group.*

The data obtained during the study show that, before the course of treatment in patients, the content of estradiol, progesterone and LH (65.7 ± 3.3 pg / ml, 1.2 ± 0.3 ng / ml and 0.31 ± 0.02 mIU / L) was statistically significantly reduced against the background of an increase in FSH, prolactin and cortisol values (27.12 ± 2.3 mIU / ml, 942.12 ± 41.2 μIU / ml and 49.5 ± 3.8 μg / dL). This is evidence of insufficient hormone-producing function of the ovaries and may be a background for a violation of the regulation of the reproductive system of a woman.
A comparative analysis of the hormone-correcting action of the applied methods of treatment revealed the undoubted advantage of using the pharmaco-physiotherapeutic method of intravaginal electrotherapy using the glutaxime preparation, which was confirmed by the restoration of the functional activity of both central and peripheral endocrine structures among the patients of the main group, whose indicators approached the norm. Thus, among women in the main group, a decrease in the level of FSH, prolactin and cortisol values to the normal level was noted (12.6 ± 0.05 mIU / ml, 412.3 ± 18.7 μIU / ml and 15.5 ± 1.5 μg / dl, respectively), respectively, with an increase in the concentration level of estradiol, progesterone and LH (223 ± 6.4 pg / ml, 14.8 ± 1.3 ng / ml and 5.7 ± 0.2 mIU / L, respectively).
A bacteriological study, carried out 14 days after the start of therapy, showed that in most of the examined women, the quality of the vaginal contents improved significantly and corresponded to the indicators of normocenosis (Table 5).

Table 5

The state of biocenosis in women with salpingoophoritis complicated by pelvic pain, depending on the type of therapy, 14 and 30 days after the start of treatment,%

Biocenosis state		14 days after treatment			30 days after treatment		
		Main group	Comparison group 1	Comparison group 2	Main group	Comparison group 1	Comparison group 2
Normocenosis	Quantity	22	17	5	33	25	7
	%	62,86	48,57	16,67	94,29	71,43	23,33
Dysbiosis	Quantity	13	18	25	2	10	23
	%	37,14	51,43	83,33	5,71	28,57	76,67

In the main group of patients, 14 days after the start of complex therapy, 37.14% of women had violations of the state of the vaginal biocenosis, while a similar result was diagnosed in the 1st comparison group in 51.43% of cases, and in the 2nd control group in 83.33% of cases.
On the 30th day after the start of complex therapy in women of the main group, dysbiotic disorders in the vagina were noted in only 5.71% of cases, while in patients of the second

group of comparison who received only basic therapy, vaginal dysbiosis was detected in 76.67% of cases. In the patients of the 1st comparison group, during the above study period, vaginal dysbiotic disorders were also found, noted in 28.57% of cases.

More than 74% of patients in the main group, 14 days after the use of complex therapy for chronic salpingo-oophoritis complicated by pelvic pain, had a significantly higher number of lactobacilli in the vaginal secretion compared with 57.14% of women in the first comparison group. When comparing the effect of treatment on the number of lactobacilli on the patients of the main group and the second group of comparison, during the study, it was revealed that 14 days after the use of complex therapy of chronic salpingo-oophoritis complicated by pelvic pain, in the second group of comparison only 40% of women had lactobacilli in the amount of 106- 108 CFU / ml.

The number of patients in the main group with normative vaginal lactoflora (91.43%) after complex therapy on the 30th day after the start of treatment was significantly higher compared to 65.71% of patients in the first comparison group. In comparison group 2, the normative parameters of lactoflora on the 30th day after the start of treatment were diagnosed in 46.67% of patients.

After the course of treatment, the patients of the main group had complaints on average in only 10% of cases, and such complaints as low-grade fever, frequent urination and impaired defecation were not observed in any patient of the main group (Fig. 2).

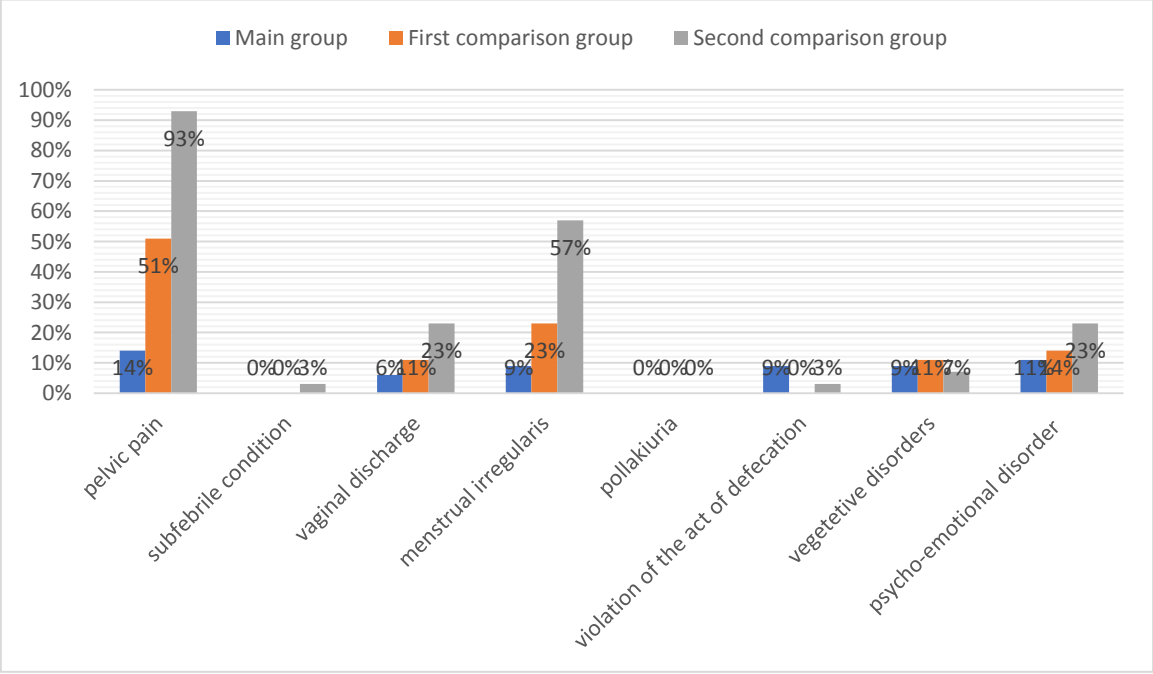

Figure: 2. Distribution of patients with chronic salpingoophoritis complicated by pelvic pain, depending on the presence of the main clinical manifestations of the disease after a course of therapy, depending on the treatment method,

In comparison group 1, despite the significant severity of regression of clinical symptoms, in 50% of cases, individual manifestations of clinical symptoms were observed, although such an important sign of the inflammatory process as subfebrile condition was also absent in patients of this group. The results obtained were significantly higher than in the 2nd comparison group, in which the regression of clinical symptoms was several times less pronounced than in the main group and in the 1st comparison group.

It should be noted that in the patients of the main group, after the course of therapy, almost all painful sensations were stopped (Fig. 3). At the same time, mild or moderate pain persisted and in the periovulatory and premenstrual periods was observed in 26% and 9% of cases, respectively, mainly in patients with a long and burdened anamnesis. Patients of the 1st and 2nd groups of comparison had a significantly less significant analgesic effect, which was confirmed by the data of the VAS pain intensity rating scale. So, slightly less satisfactory results than in the main group were achieved in patients receiving treatment based on ultrasound therapy.

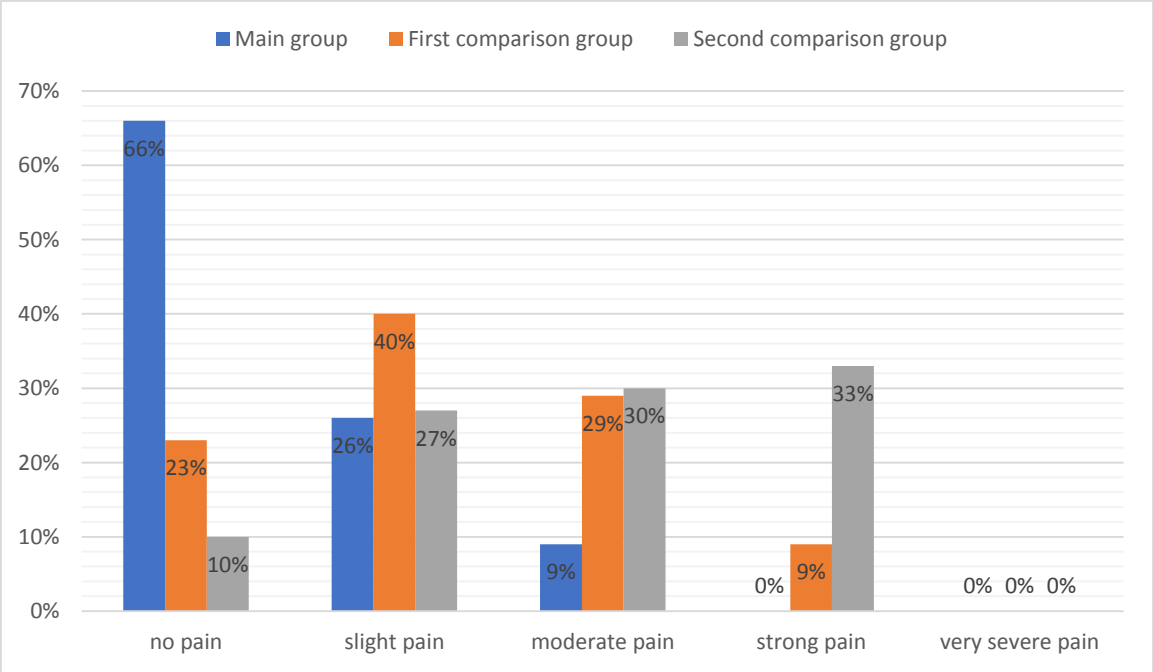

Figure: 3. Distribution of patients with chronic salpingo-oophoritis complicated by pelvic pain, depending on the intensity of pain on the VAS scale after the course of therapy,%

Thus, according to the results of the comparison of the three treatment regimens, it can be noted that there is an anti-inflammatory effect, a positive effect on hormonal status and the therapeutic efficacy of intravaginal electrotherapy in patients with chronic salpingoophoritis complicated by pelvic pain, which is statistically confirmed.

4. CONCLUSIONS

After analyzing all the data, we came to the following conclusions:

1. The clinical efficacy of the applied methods of treatment was assessed on the basis of a combined analysis of the regression of clinical symptoms and the dynamics of special research methods, as a result of which, with a high degree of reliability, the advantage of using the developed pharmaco-physiotherapeutic method (91%) in comparison with intravaginal ultrasound therapy was proved (74 %) and, especially, drug therapy (40%).
2. The use of intravaginal electrotherapy with the use of glutoxim contributes to a more pronounced relief of all clinical symptoms and, which is especially important, of chronic pain syndrome in patients with chronic salpingoophoritis, the intensity of which decreases to the minimum values on the VAS scale.
3. The developed method of intravaginal electrotherapy using glutoxim has a pronounced anti-inflammatory effect, which is confirmed by the results of bimanual and intravaginal ultrasound in the form of a decrease in the size of the uterine appendages and an increase in their mobility in patients with chronic salpingoophoritis complicated by chronic pain.

4. In patients with chronic salpingoophoritis, complicated by chronic pain, under the influence of intravaginal electrotherapy using glutoxim, the functional state of the central and peripheral endocrine structures improves, which is confirmed by the restoration of the level of sex hormones (estradiol, progesterone, LH, FSH, prolactin and cortin) to the physiological norm. ...

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