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PECULIARITIES OF TREATMENT AND PREVENTION OF RECURRENCES IN WOMEN WITH INTRAUTERINE PATHOLOGIES

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Abstract

The study is devoted to the problem of surgical treatment, rehabilitation program and prevention of recurrences in intrauterine pathologies (polyposis and uterine adhesion) in women with reduced reproductive potential. The urgency of this problem is characterized by a high frequency of abnormal uterine bleeding, hypomenstrual syndrome and amenorrhea, infertility and miscarriage. Clinical data include the own experience of treatment and rehabilitation of 66 patients; women with intrauterine synechiae (32 people) were included in group 1; 34 patients with hyperplastic form of chronic endometritis and polyposis were included in group 2. The control group included 30 healthy patients without gynecological pathology and menstrual irregularities. All women underwent therapeutic hysteroscopy with adgeolysis and polypectomy. In the postoperative period, 24 patients of the main group received the proposed program to restore the endometrium and its implantation potential. The comparison group included 42 patients with general principles of postoperative management. The key points of the proposed program were: immunomodulatory therapy, hormone replacement therapy and the use of autoplasm. As a result of the study, a reduction in the recurrence of the adhesive process was proved, as well as a significantly higher number of cases of pregnancy. Thus, for the comprehensive treatment of intrauterine pathology in young

women with reduced reproductive potential it is important not only to use minimally invasive office hysteroscopy, an active postoperative rehabilitation period is of great importance too.

Key words: intrauterine synechiae; hyperplastic form of chronic endometritis; office hysteroscopy; autoplasm platelets.

Topicality. Prevention of infertility as well as restoration of fertility are priority areas in modern medicine, as the incidence of infertility among couples today reaches 18-20%, which exacerbates the socio-demographic crisis nationwide and preserves the importance of the problem in medical and socio-economic aspects [1, 3, 15, 17]. The development of assisted reproductive technologies and the improvement of approaches in this area, without a doubt, increases the likelihood of pregnancy and the birth of healthy children in couples with various causes of male or female infertility. One of the ways to improve reproductive health in women suffering from infertility is to optimize the conditions of embryo implantation, as the adequate implantation capacity of the endometrium with a correct, complete and scrupulous implementation of protocols and techniques of assisted reproductive technologies provides a probability of getting pregnant [8-12, 16].

Decreased fertility is due to a significant number of reasons, but the share of uterine factors in both isolated and combined version accounts for 24-62% [3, 5-7, 13, 14]. Reproductive dysfunction is the result of many reasons, but the uterine factor in their structure is of great importance – 24-62%, which undoubtedly contributes to an increase in ectopic pregnancy, habitual miscarriage, premature birth and abnormal localization of the placenta [3, 5]. A number of epidemiological studies conducted in many countries around the world show that the leading causes of impaired generative function of women are morphofunctional changes of the endometrium, such as chronic endometritis, intrauterine synechiae, polyposis and hyperplastic processes in more than half of the examined patients (54%), as well as structural and functional changes in the endometrium, which may be an independent cause of reproductive dysfunction: disorders of subendometrial blood flow, endometrial dyschronosis, sclerotic and immunological changes [3, 5-7].

All of the above puts before practical medicine the task of finding ways to optimize rehabilitation measures and improve the implantation ability of the endometrium, which was the purpose of this study.

Materials and methods. The paper presents an analysis of monitoring and treatment of 66 patients with intrauterine pathology who underwent surgery; they were divided into two groups: 32 patients with uterine synechiae and 34 patients with endometrial polyposis. The

depth of the pathological process in the uterine cavity, in particular intrauterine synechiae, was assessed during office diagnostic hysteroscopy according to the classification of the European Association of Gynecologists and Endoscopists (ESH, 1989). The B.I.O.H. (Karl Storz) surgical hysteroscope was used for office hysteroscopy. According to the severity, the intrauterine synechiae were of the first and second degree in equal proportions. All patients underwent hysteroscopy using an office hysteroscope and underwent intrauterine adgeolysis and polypectomy with resection of the hyperplastic endometrium. When performing hysteroscopy in patients with uterine synechiae, certain technical features were observed: the manipulation was performed without dilation of the cervical canal and probing of the uterine cavity by “no-touch” technology according to S. Betocchi [2, 15], under visual control with a constant supply of fluid to expand the uterine cavity, tender and single synechiae were separated by hydraulic dissection, in case of failure – by hysteroscopic scissors and forceps, in case of fibrosis of adhesions the hysteroresection and adheolysis were performed using a rigid hysteroresectoscope and bipolar electricity in accordance with the concept of “See and treat” under the control of ultrasound. During hysteroscopy, the majority of patients underwent adgeolysis by hydraulic dissection, a third of patients – using hysteroscopic scissors, and 7 women (21.9%) underwent additional resection of synechiae using a bipolar hysteroresectoscope (Karl Storges) due to dense fibrous adhesions, in half of the cases – under the control of ultrasound.

However, it should be noted that even very careful and professional surgery keeps the risk of recurrence quite high – up to 30.9%, which indicates the feasibility of preventive measures in the postoperative period. An important and necessary step in restoring the functional ability of the endometrium is careful and thorough manipulation with the preservation of the islands of the functioning endometrium which are necessary for its regeneration, as well as the endometrial recovery program, which provides cyclic hormone therapy for three menstrual cycles, optimization of rehabilitation measures and, if necessary, control diagnostic hysteroscopy.

The proposed rehabilitation program was used in 24 patients (main group) and included the following points, which were formed using a personalized approach. In the postoperative period, the program of therapeutic options included immunomodulatory agent galavit 0.2 g/m 1 time per day for 2 days, then 0.1 g i/m 1 time per day for 10 days; for recovery and regeneration of the endometrium – cyclic hormone therapy for 3 months (estradiol (1 g per skin 1 time per day or 1 tablet per os 1 time per day) from the 5th to the 15th day of MC with the addition of micronized progesterone 200 mg 3 times a day intravaginally

from the 16th to the 25th day of MC, in case of morphofunctional disparity of the endometrium and phase of MC – 3 months of low-dose COCs with a high antiproliferative index. An additional option was using of chronic endometritis in the verification (according to immunohistochemical studies) – platelet-containing autoplasm injections. Platelet-containing autoplasm was administered intrauterinely in an amount of 0.5-1 ml. Quincke’s needle was used not only to install platelet-enriched autoplasm, but also to scratch the basal layer of the endometrium at the same time, starting from the area of the internal orifice distally to the bottom of the uterus along its posterior wall. Then a similar manipulation was performed from the mouth of one fallopian tube to another one. At the same time, platelet-containing autoplasm microinjections were made paracervically to a depth of 0.5 cm, in the submucosal layer 1.5 ml on both sides. This therapeutic option was carried out after informing the patient about the feasibility of its use, as well as signing an informed consent to the manipulation. Platelet-containing autoplasm is non-toxic and immunoreactive, it accelerates natural regeneration mechanisms due to the presence of growth factors and modulating the function of primary growth factors [8-10, 16]. This manipulation was performed after hysteroresectoscopy and twice more during cyclic hormone therapy in the late phase of proliferation during three menstrual cycles. The advantage of this method is the strengthening of blood supply, anti-inflammatory effect which implements the principles “proliferation without inflammation” [8-10, 16].

Research results and their discussion. Most often, patients complain of hypomenstrual syndrome, abnormal uterine bleeding, dysmenorrhea, chronic pelvic pain syndrome, infertility and miscarriage (Table 1).

Table 1

The most frequent complaints of patients of the studied groups, abs.freq.,%

Values	Studied groups of women						Significance of differences, P
	Group I, n=32, abs.freq.,%		Group II, n=34, abs.freq.,%		Control group, n=30, abs.freq.,%		
	Abs.freq.	%	Abs.freq.	%	Abs.freq.	%	
Oligoopsomenorrhea	12	37.5	-	-	-	-	P _{1,2} < 0.05
Uterine bleeding	3	9.3	18	52.9	-	-	P _{1,2} < 0.05
Amenorrhea	15	46.9	5	14.7	-	-	P _{1,2} < 0.05
Algodysmenorrhea	14	43.8	13	38.2	1	3.3	P ₂ > 0.05
Chronic pelvic pain syndrome	7	21.9	8	23.5	-	-	P ₂ > 0.05

Notes: P1 – the difference is significant relative to the control values, P2 – the difference is significant relative to the values of group 1, p <0.05.

The calculations revealed a high proportion of opsomenorrhea (37.5%), as well as a significant proportion of secondary amenorrhea in the first group; meno-metrorrhagia and intermenstrual bleeding (52.9%) – in the second group, which indicates the development of transformation processes of the endometrium in the case of uterine factor compared with control data and between groups, respectively ($p < 0.05$). A moderate correlation ($r = 0.42$) was determined between the development of intrauterine adhesion and the presence of abortions.

As shown in Table 2, almost all patients included in the study had a history of instrumental interventions (scraping of the uterine cavity, abortion, two-thirds of the patients had diagnostic hysteroscopy, every third woman has already undergone hysteroresectoscopy or adhesiotomy with repeated use of therapeutic options for endometrial rehabilitation. In addition, episodes of retrochorial hematomas, miscarriage, and failed IVF attempts were more common in this category of patients.

Table 2

Characteristics of the anamnesis in the examined groups, abs.freq.,%

Values	Group I, n=32, abs.freq.,%		Group II, n=34, abs.freq.,%		Significance of differences, P
	Abs.freq.	%	Abs.freq.	%	
Instrumental interventions	32	100.0	21	61.8	$P_1 < 0.05$
Diagnostic hysteroscopy	23	71.9	23	67.6	$P_1 > 0.05$
Adgeodisis, polypectomy	12	37.5	13	38.2	$P_1 > 0.05$
Failed IVF	7	21.9	5	14.7	$P_1 < 0.05$
Miscarriage	7	21.9*	7	20.6*°	$P_1 > 0.05$

Note. P1 – the difference is significant relative to the values of group 1.

It should be noted that according to morphological and immunohistochemical studies of endometrial biopsy, in all studies the signs of chronic endometritis were described which indicated profound morphofunctional changes in the structure of the endomyometrium and required a long-term rehabilitation for at least three monthly cycles.

After medical hysteroscopy, regular menstrual function was restored in more than half of the cases. In 11 patients with secondary amenorrhea, there were minor menstrual discharge; dysmenorrhea was revealed in 13 patients. Recurrences of the adhesive process were noted only in 2 patients (8.3%) of the main group, while in the comparison group (42 women) the recurrence of synechiae and polyposis was noted in 35.7% (15 observations), mainly in women with severe course of the disease.

All patients were preparing to use the IVF program. Data on the restoration of reproductive potential, presented in Table 3, showed significant positive results in patients of the main group, where pregnancy was noted significantly more often ($P_1 < 0.05$) – in more than half of the observations, with one in three being spontaneous, while in the comparison group, almost all patients used assisted reproductive technologies.

Table 3

Reproductive function after rehabilitation therapy in patients of the examined groups, abs.freq.,%

Values	Main group, n=24, abs.freq.,%		Comparison group, n=42, abs.freq.,%		Significance of differences, P
	Abs.freq.	%	Abs.freq.	%	
Pregnancy, including:	13	54.2	12	28.6	$P_1 < 0.05$
Timely live birth	7	53.8	4	33.3	$P_1 > 0.05$
Missed miscarriage	2	15.4	4	33.3	$P_1 > 0.05$
Spontaneous miscarriage	2	15.4	3	25.0	$P_1 < 0.05$
Premature birth	2	15.4	-	-	$P_1 > 0.05$

Note. P_1 – the difference is significant relative to the values of the comparison group.

Conclusions. Thus, a comprehensive approach to the diagnosis, treatment and monitoring of patients with reduced reproductive potential due to intrauterine factor (adhesive process, hyperplastic form of chronic endometritis) requires a careful, professional and thorough approach to the choice of surgical intervention method, where preference should be given to office minimally invasive technology. Important aspects of postoperative support are therapeutic options aimed at preventing recurrence, restoring the functional state of the endometrium, and restoring its receptivity. The use of the proposed program of application of the procedure of injection scratching of autoplasm with platelets in combination with hormone therapy can be considered as a modern innovative approach to the prevention of uterine adhesion and endometrial hypoplasia with a high percentage of success in restoring fertility. At the same time it is necessary to keep the personalized approach taking into account all features of the morphofunctional characteristic of the endometrium.

Future studies of the molecular mechanisms of endometrial regeneration in infertile patients are promising.

Conflict of interest: the authors declare no conflict of interest during the writing of this article.

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