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UTRASONOGRAPHIC MONITORING OF UTERINE MOTILITY IN INFERTILE WOMEN WITH ADENOMYOSIS

УЛЬТРАСОНОГРАФИЧЕСКИЙ МОНИТОРИНГ МАТОЧНОЙ ПЕРИСТАЛЬТИКИ У БЕСПЛОДНЫХ ЖЕНЩИН С АДЕНОМИОЗОМ

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Abstract

Taking into account that the uterine pump disruption is one of the leading pathogenic links of infertility in external endometriosis, a significant role of this factor can be detected and in adenomyosis. Diagnosis of uterine peristalsis held with ultrasonography (US), and the study of intrauterine transport was made by hysterosalpingoscintigraphy. Disperistaltic waves at were revealed predominantly in periovulatory phase with the average rate of 4.8 ± 0.23 waves / min. In the control group only single disperistaltic waves throughout the cycle, and their frequency did not exceed 0.4 ± 0.11 waves / min. In all the women with the lack of intrauterine transport either disperistaltic or complete absence of subendometrial layers of myometrium contractions wave were found. The significant increase of hysterosalpingoscintigraphy negative results and contralateral transport depending on the patients' age was revealed ($p < 0.01$ and $p < 0.05$, respectively). Therefore, patients with adenomyosis and impaired uterine peristaltic older than 30 years old should be recommended

one of the techniques of extracorporeal fertilization with embryo transfer technology, except for intrauterine insemination.

Key words: adenomyosis, infertility, uterine pump, uterine peristalsis.

Реферат

Учитывая, что нарушение работы маточной помпы - одно из ведущих звеньев патогенеза бесплодия при наружном эндометриозе, может быть обнаружена значимая роль этого фактора и при аденомиозе. Диагностика маточной перистальтики проводится при ультразвукографии (УЗИ), а исследование внутриматочного транспорта – методом гистеросальпингосцинтиграфии (ГССГ). Дисперистальтические волны при аденомиозе обнаружены преимущественно в периовуляторной фазе со средней частотой $4,8 \pm 0,23$ волн/мин. В контрольной группе наблюдались только единичные дисперистальтические волны на протяжении всего цикла и их частота не превышала $0,4 \pm 0,11$ волн/мин. У всех женщин с отсутствием внутриматочного транспорта обнаружены дисперистальтика или полное отсутствие волн сокращения субэндометриальных слоев миометрия. В ходе исследований обнаружено, достоверное увеличение числа случаев отрицательных результатов ГССГ и контралатерального транспорта с возрастом пациенток ($p < 0,01$ и $p < 0,05$, соответственно). Поэтому пациенткам с аденомиозом и нарушением маточной перистальтики старше 30 лет следует рекомендовать одну из методик экстракорпорального оплодотворения с технологией переноса эмбриона, исключая внутриматочную инсеминацию.

Ключевые слова: аденомиоз, бесплодие, маточная помпа, маточная перистальтика.

Adenomyosis is one of the most common gynecological diseases often seen in women with reduced fertility. The frequency of adenomyosis in women of reproductive age, according to different researchers, varies from 12 to 40% [1, 5, 6, 7, 8]. The frequency of infertility ranges from 12 to 50%, which is often caused by a variety of pelvic or other factors not directly related to adenomyosis [1, 2, 7, 8, 9]. But in practice there are cases when in-depth survey of patients with adenomyosis can not detect any factor infertility.

The studies of S. Kissler, A. Zeitvogel, R. Bauman, V. N. Zaporozhan made in 2000-2006 [7, 13, 17], manage to prove that in external endometriosis patients one of the leading pathogenesis of infertility is a disruption of the uterine pump. The working hypothesis of this

study was the assumption of the possible presence of violations of the uterine motility in infertile women with adenomyosis.

At the present stage, diagnosis of uterine peristalsis can be made by dynamic ultrasonography, and the study of intrauterine transport - by hysterosalpingoscintigraphy [7, 13].

The objective: to investigate the characteristics of the uterine motility in infertile women with adenomyosis by dynamic ultrasonography.

Material and methods. 85 patients with adenomyosis of the I-III stage and both without comorbidities or with uterine myoma of small size (up to 20 mm) have been examined. They composed the treatment group. The group of comparison was made up of the women with only male factor infertility (32 patients) in a pair. The distribution of patients by age is shown in Table 1.

Inclusion criteria were: absence of severe concomitant extragenital pathology, stage adenomyosis stage not higher than the IIIrd, duration of afetal period not less than 2 years, age of 22-45 years old. The study included only the women with concomitant uterine myoma, which could not have a significant impact on the development of infertility (subserous or intramural nodes up to 20 mm, which do not distort the uterine cavity). All patients underwent a complete clinical and laboratory examination, hysteroscopy, endometrial biopsy with histological analysis.

All the patients under examination went diagnostic laparoscopy which allowed to exclude tubal factor and external endometriosis.

Diagnosis of adenomyosis was made at ultrasonography with color Doppler mapping on the device Sonoline G-40 (Siemens), in some patients magnetic resonance imaging at the tomograph XGY Oper 0.4 (Ningbo Xingaoyi Medical Instruments Co., Ltd.), hysteroscopy and laparoscopy at of KARL STORZ equipment have been performed. Diagnosis of uterine myoma was performed by transvaginal ultrasonography at Sonoline G-40 (Siemens), vaginal probe 7.5 MHz.

Registration of contractile activity of myometrium subendometrial layers was carried out with ultrasound in sagittal projection of the entire uterus and fixed for 5 minutes position with video-recording of the whole scanning procedure. The direction of peristaltic waves (either cervicofundal or fundocervical) was differentiated by the method described by Lyons E. A. (1991), [15]. Myometrium peristaltic waves were recorded five times at 2, 7, 12, 16 and 22 days of the cycle.

Hysterosalpingoscintigraphy (HSSG) was carried out in the preovulatory phase, after the ultrasonic identification of the dominant follicle. The survey was performed according to W. Becker and T. Steck, with R. Kissler's modification (2000) by scanning at gamma camera "General Electric" DST XLJ for 30 minutes after the administration of the catheter to the *os uteri internal* of 0.2-0.5 ml albumin microspheres labeled in the radionuclide camera by technetium Tc^{99m} radioisotope with emission of 10-35 MBq [13]. Pulmocis "CIS bio international, Schering SA" (Germany) and SolcoMAA "Solco Basel AG, Birsfelden" (Switzerland) were used.

HSSG results evaluation was conducted on a computer by SPSS Windows 2007 ("SPSS Inc.", Chicago, Illinois) program according to S. Kissler's et al. recommendations (2001) [13].

Results and discussion.

Only reproductive age patients (33.1 ± 3.6 years) were included into the study. The duration of their specified period of infertility averaged 4.6 ± 1.1 years. 74.3% of the treatment group patients had primary infertility.

The data on the concomitant extragenital pathology in the treatment and comparison group patients are given in Table 2. Statistically significant higher morbidity rate of the nervous system and thyroid gland ($p < 0.05$ and $p < 0.05$, respectively) pathology has been revealed in the adenomyosis patients as compared with the control group.

Table 1.

Distribution of the patients by age in the treatment and control groups

Group	Age, years						n
	<30 (n=44)		31-35 (n=86)		>36 (n=88)		
	abs.	%	abs.	%	Abs.	%	
Treatment group	18	21,2	40	47,0	27	31,8	85
Control group	7	21,9	12	37,5	13	40,6	32

Table 2

Co-morbidity rate in the patients of the treatment and control groups

Group of pathology	Main group		Control group	
	abs.	%	Abs.	%
Gastrointestinal diseases	24	28,2	7	21,9
Hepatic disorders	21	24,7	5	15,6
Cardio-vascular diseases	16	18,8	4	12,5
Respiratory diseases	11	12,9	3	9,4
Nervous system diseases	42	49,4	6	18,8
Excretory system diseases	14	16,5	1	3,1
Thyroid gland disorders	23	27,1	2	6,3
Ophthalmological diseases	7	8,2	3	9,4
intolerance to drugs and food items	19	22,4	4	12,5

Features of uterine peristalsis in all the patients under examination are shown in Fig. 1 and Fig. 2.

While investigating uterine contractions, we found statistically significant ($\chi^2 = 0.87$, $p < 0.05$) increase of peristaltic waves frequency in the treatment group patients under control group almost throughout the cycle. In this regard disperistaltic waves were observed only in 19% of control group patients, and in 94% of the treatment group patients ($p < 0.01$).

Disperistaltic waves in adenomyosis patients were found predominantly in peri-ovulatory phase with the average frequency 4.8 ± 0.23 waves per minute. Only two control group patients had isolated disperistaltic waves observed throughout the cycle, and their number does not exceed 0.4 ± 0.11 waves per minute, which was significantly less ($\chi^2 = 0,72$), than in the treatment group.

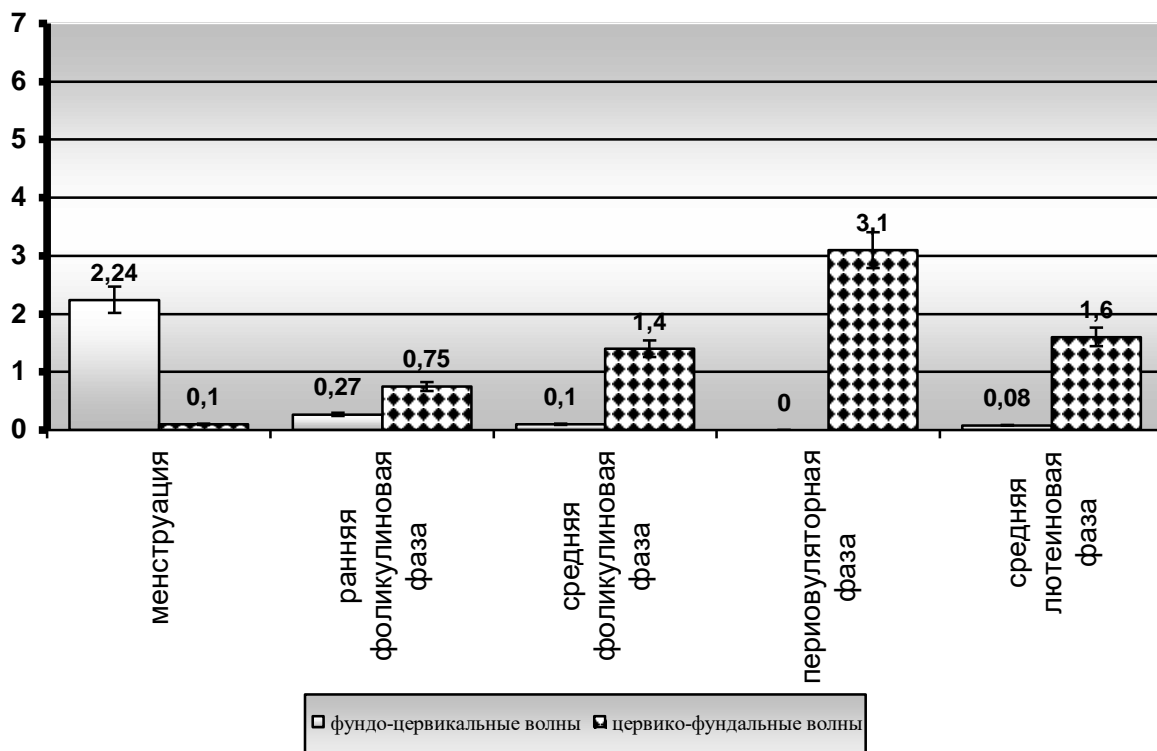


Fig. 1. Uterine peristalsis in healthy women of control group, frequency of waves per minute

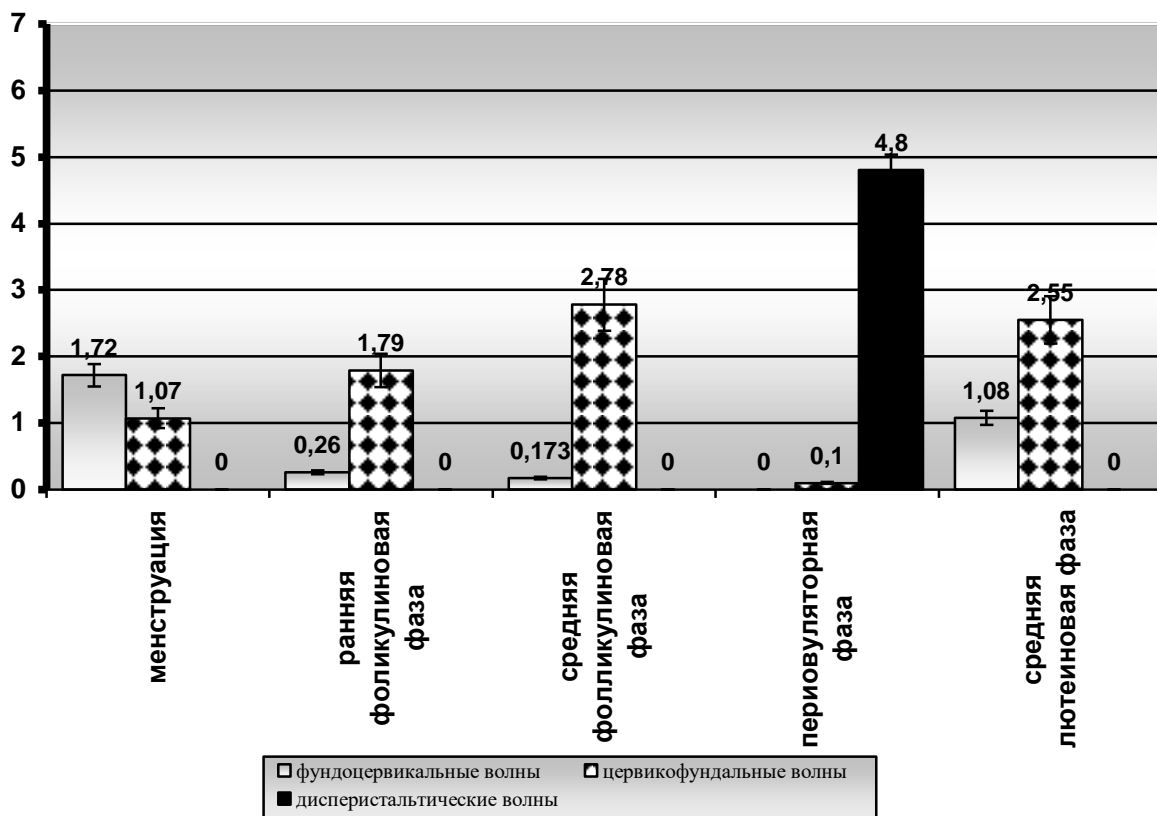


Fig. 2. Uterine peristalsis in adenomyosis patients, frequency of waves per minute

All the patients with the frequency of disperistaltic waves above 1.6 ± 0.17 per minute there was either moderate or severe chronic pelvic pain syndrome. At the waves frequency below 0.8 ± 0.14 per minute none of the patients complained of algomenorrhea, dyspareunia or chronic pelvic pain.

The results obtained indicate a pronounced violation of the contractile activity of the myometrium subendometrial layers at adenomyosis.

The question of what comes first: motility disorders of the uterus or the development of adenomyosis microcenters violating the contractile activity of the myometrium, is debated. We can assume that disperistaltic waves appear in violation of the intercellular transmission of the contractile impulse as a result of changes in the properties such as cell-cell contact of Zona adherens type by substituting in them Class E catherines by those of Class N [16]. In turn, hyper- and disperistalsis lead to divergence of endometrium basal layer cells, endometrial and myometrium cytoarchitectonics violations. This leads to microtrauma and disintegration of endometrial basement membrane and may be a trigger for the cascade of reactions that lead to the penetration of endometrium basal layer cells under basal membrane and activation of N-catherine-synthesizing system while suppressing the synthesis of apoptosis mediators. It is the appearance of N-caterinas causes the appearance of pathological adhesion properties in the basal layer endometrium cells and stimulates adenomyosis development. The results of R. Baumann's A. Starzinski-Powitz's researches (2000-2004) may support the hypothesis offered. The researches' mentioned a statistically significant higher levels of N-catherines in endometrium of adenomyosis patients than in the healthy subjects [16, 17] have revealed. Perhaps that is N-catherines are major predictors and markers for adenomyosis, but this requires further experimental studies.

Thus, we have found a violation of uterine peristalsis in adenomyosis as active disperistaltic waves which almost never occur in healthy women.

In some of both groups patients (43 patients of the treatment and 19 patients of the control group) hysterosalpingoscintigraphy was held. According to a survey the treatment group patients were divided into 4 subgroups:

- (a) Ipsilateral transport - 7 women;
- (b) Bilateral intrauterine transport - 8 women;
- (c) Contralateral intrauterine transport - 11 women;
- (d) The absence of intrauterine transport - 17 women.

Intrauterine transport disorders and its complete absence were found in adenomyosis women (68%) and the control group patients, but more rarely (21%). 15 women of the control group had HSSG's diagnosed ipsilateral transport, 2 had bilateral one, contralateral transport had one person and 1 patient had no endometrial transport. Ultrasound examination revealed disperistaltic waves only in 2 control group patients. At the same time, one of them had no intrauterine transport, while the second had ipsilateral one. Our data for normal fertility patients without adenomyosis correspond to the data of Kunz et al. (1996) [14].

We found that the frequency of HSSG negative results at adenomyosis is 39.5%, which is almost 8 times more ($p < 0.01$), than in the group of healthy women. This, of course, speaks in favor of our hypothesis about the importance of intrauterine disorders of sperm transport in the pathogenesis of infertility at adenomyosis. In addition, it was found that at adenomyosis transport to the contralateral tube is 5 times more often, at 25.6% of the patients ($p < 0.05$), and bilateral transport occurs twice as often at 18.6% of sick persons ($p < 0.05$) than in the control group. These data indicate significant changes of subendometrial layers of myometrium peristaltic waves tropism.

The studies detected that the number of HSSG negative results and contralateral transport significantly increases with the age of patients ($p < 0.01$ and $p < 0.05$, respectively). Neither of the patients above 36 years old had normal ipsilateral transport. Similar results were obtained in studies of S. Kissler et al. (2002) at the examination of idiopathic infertility patients [13].

Comparison of ultrasound and HSSG has revealed violations of contractile function of the uterus in the form of disperistalsis or a complete lack of subendometrial layers of the myometrium waves contraction in all the women with the absence of intrauterine transport. However, not all disperilstalsis women had violations of intrauterine transport.

In patients with ultrasound myometrium contractions more than 4 per minute, significantly more often ($p < 0.05$) bilateral intrauterine transport was revealed, but not all patients with bilateral transport detected abnormalities in contractile function of the uterus at ultrasound examination.

There were no significant differences in uterine contractive activity in patients with contralateral intrauterine transport, which may indicate the presence of other causes of the uterine's pump disruption.

Considering previously published data of retrospective analysis of reproductive outcomes in patients with various disorders of intrauterine transport [10], the results of this study suggest that the effectiveness of conservative methods of rehabilitation of reproductive

function in infertile patients above 30 years old with adenomyosis and infertility duration more than 3 years are questionable enough. At infertility of more than 5 years the onset of spontaneous pregnancy in the patients above 36 years old is unlikely. Therefore, adenomyosis and impaired uterine peristalsis patients above 30 years old should be recommended one of in vitro fertilization techniques with embryo transfer, with the exception of intrauterine insemination.

Based on the data found, we can assume that violation of myometrium subendometrial layers peristalsis violations, along with other age-dependent factors is one of the important mechanisms of fertility reduction in late reproductive age adenomyosis women.

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