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EVALUATION OF PRECONCEPTION PREPARATION IN PREVENTION OF COMPLICATED GESTATION IN WOMEN AFTER MYOMECTOMY

ABSTRACT

We examined 300 women with uterine fibroids and carried out over the next 12-24 months myomectomy, 150 of which had preconception care (treatment), 150 - not. The average age of women - 33,4±3,2 years, duration of disease (uterine fibroids) - 4,25 ± 1,4 years. The comparative evaluation of the effectiveness of preconception care in the prevention of complications of pregnancy in women after myomectomy is presented.

Keywords: uterine fibroids, myomectomy, preconception care.

INTRODUCTION

Uterine fibroids is diagnosed in 25-30% of women over the age of 35 years [16,1]. Uterine fibroid in some cases requires surgical or pharmacological treatment [5,8]. The basic task of gynecology is sparing treatment of uterine fibroid patients, which use a variety of methods (myomectomy, embolization of the uterine vessels, focused ultrasound ablation controlled by magnetic resonance imaging, anti-recurrence pharmacotherapy and others.) [6,5]. However, to exclude recurrence of uterine fibroid, inefficiency of the chosen method of therapy, unwanted side effects are possible, which is especially important for women planning pregnancy [6, 2,3, 4,5].

Hitherto proposed various recommendations on preconception preparation of women with different pathologies [4, 9, 10,11]. However, there is no uniform guidelines for preconception preparation of women with uterine fibroid who underwent different treatment methods. In the international literature accumulated clinical experience on the specifics of the prediction, diagnosis and treatment of gestational complications in women with uterine fibroid [7,3].

Objective: To estimate the effectiveness of preconception preparation in the prevention of complications of gestation in women after myomectomy.

MATERIALS AND METHODS

Presented by the non-randomized, controlled, open-label study of 300 women with uterine fibroid and conducted previously myomectomy. Criteria for inclusion in the study: the reproductive age; uterine fibroids; myomectomy, produced over the next 12-24 months; spontaneous pregnancy without assisted reproductive technologies; a history of infertility or miscarriage as a result of the uterine fibroid; late reproductive age (limited time for attempts to implement fertility). The average age of the women studied was 33,4□3,2 years, duration of disease uterine fibroid - 4,25 ± 1,4 years. Depending on preconception preparation was carried out or not, the women were divided into two clinical Groups. In the clinical Group I were included 150 women, which after myomectomy undergo preconception preparation. In the clinical Group II included 150 women who after myomectomy has not been evaluated preconception preparation. The sample of women with inclusion criteria was conducted in antenatal clinics in Krasnodar and Novorossiysk. Examination and treatment was carried out on the bases of Krasnodar: gynecological department of the «Regional Clinical Hospital №2» Perinatal center, gynecological department the «Maternity» №4, and Novorossiysk: gynecological department of the «Perinatal Center» from 2010 to 2014 .

Women in both Groups were comparable in age, gynecological, obstetrical and extragenital pathology.

The women in the Group I surgical treatment within the scope of myomectomy was performed by the authors endoscopic access routinely: the interstitial - submucous and submucous - interstitial localization (with a little interstitial component) by hysteroscopic resectoscope in other cases by laparoscopy (subserous nodes on the stem, subserous - with little interstitial interstitial component) with the imposition of endoscopic sutures, comparing the maximum wound surfaces on the uterus. The dynamics performed transvaginal ultrasound access.

Women of the Group II as surgery performed endoscopic access routinely in the amount of myomectomy. All women of this group of myomectomy was performed in different hospitals of Krasnodar, Krasnodar Territory (Krai), Russia. Information about the uterine fibroid features (number of nodes, their location, volume of the uterus, etc.) before and after myomectomy was obtained from medical records (outpatients, in-patient cards, ultrasound protocols, operations). Some women in the clinical the Group II ignored the recommendations proposed by him after myomectomy for anti-recurrence therapy of uterine fibroid, and pregnancy who just came spontaneously.

Women of the Group I performed immunohistochemical study of fibroids removed, determines the frequency of detection of mutations in the p53 factor Bcl-2 and Ki-67 expression intensity of Bcl-2 factor.

After myomectomy to defer pregnancy for the regeneration of the myometrium, endometrium, anti-recurrence treatment of uterine fibroid appointed micro doze combined oral contraceptives (COCs) for a period of 9-12 months.

Preconception training included the B vitamins (B6 and B12), folic acid, omega-3 polyunsaturated fatty acids, progesterone (Dydrogesterone 20 mg per day during the second phase of the cycle) was performed 2-3 months before the expected reproductive cycle.

For the statistical analysis of the results of the study used statistical package SPSS v15.0, Microsoft Excel 2007. Were

calculated: the numerical characteristics of a variation number (N - number of women; M - the average (mean), m - standard error of the mean; the accuracy of the various samples (p) on t - t-test; relative risk (relative risk, RR) with 95% confidence interval (lower and upper limits of the 95% CI (confidence interval, CI), sensitivity (Se) and specificity (Sp) In order to assess the effectiveness of preconception preparation. It calculated the number of patients needed to treat, (number needed to treat, NNT) - one of the indicators of treatment (number of women with uterine fibroid who need to make preconception preparation for the prevention of gestational complications).

RESULTS

In studying the anamnesis of the disease uterine fibroid main complaints were determined to appeal to a gynecologist. In 62% of the women was a violation of the basic premise of menstrual-ovarian function in 85% - characteristic pain syndrome, 10% had been diagnosed violation of fibroid node power, 24% of impaired function of adjacent organs. At the absolute number of women (100%) of uterine fibroids is the dominant factor infertility.

In studying the characteristics of reproductive function was found out that only 60% of women in the Group II had a history of childbirth, 20% of women suffering from infertility, 16% of spontaneous abortions were noted. Noteworthy is a history in 76% of women surveyed artificial abortion, indicating that the undisciplined, uncontrolled regard to the majority of women to their own reproductive function. The number of abortions per woman was 3.73 + 2.09. Just when analyzing contraceptive history revealed that the COC took only 12% of women, and advantageous methods of contraception were selected barrier method (male condom), coitus interruptus, the rhythm (calendar, biological, thermal) method.

Initial size (before myomectomy) of fibroids were similar in both Groups, reached in a maximum diameter of 110 mm (45,82 ± 20,76 mm). The number of nodes per woman were from 3 to 11 (5,18 ± 2,5). Among them: subserous-interstitial - 4,8 ± 0,51, subserous - 1,46 ± 0,34, interstitial - 1,0 ± 2,05. After myomectomy number of not removed fibroid nodes for various reasons (small size and interstitial localization, localization in the vascular bundles of the uterus) was 3-5, the dimensions of which do not exceed 15 mm.

Immunohistochemical study of removed fibroid nodes at the Group I found out, the detection rate of p53 mutation was 21,4%, Bcl-2 - 85,7%, Ki-67 - 64%. In the presence of mutations in Bcl-2 expression intensity of this factor of 54% was poor, 46% - intensive.

It was evaluated the time interval between the end of treatment and the onset of pregnancy (in the Group I after cessation of COCs, in the Group II - after myomectomy). In the Group I it was 2.8 on the average (1 to 5) months, in the Group II - 6 (1 to 14) months. It should be noted that in one case in the Group II the pregnancy after myomectomy in the subsequent menstrual cycle, and the first time a woman went to the doctor of female consultation in pregnancy of 15 weeks.

An ultrasound of the uterine scar after myomectomy in women in thr Group I in the preconception period in the myometrium visualized structure without clear contours, medium echogenicity with point hyperechoic inclusions (presumably - suture material) loci with or without blood flow loci. Loci blood flow were determined up to 3 months after myomectomy, 6 months later is not determined by any one woman.

In the 1st trimester of pregnancy based on the utero-chorionic Doppler circulation in women of the Group I vascularity index (VI) was 6.4 in the central zone; in the paracentral zone - 6.0; 6.2 in the peripheral area. In women of the GGroup II the same Doppler parameters were as follows: in the central zone of VI was 5.7; in the paracentral zone - 5.0; 4.52 in the peripheral zone. This difference was seen as a lack of sufficient heteromorphism vascular tissue forming the placenta as ultrasound marker of the risk of primary placental insufficiency.

In assessing the complications of gestation revealed that in the I trimester of pregnancy (Table 1). Group II women threatening miscarriage rate was significantly higher (t = 3.15; RR 1.719 [1.332-2.219]; NNT = 3.984; Se 0.634; Sp 0.618). In Group II, in some cases required hospitalization up to 25 days. Ultrasound signs of detachment of chorionic varying severity in both Groups revealed a comparable frequency. Noteworthy is that 12% of women in Group I and 14% of women of Group II in the 1st trimester of pregnancy revealed iron deficiency anemia mild.

Analysis of complications of gestation in the II trimester of pregnancy (Table 2) found a higher incidence of threatening (t = 3.97; RR 3.0 [1.959-4.594]; NNT = 3.409; Se 0.750; Sp 0.604) miscarriage women Group II. In addition, the ultrasound showed signs of placental abnormalities in 2% of women .

The course of pregnancy in women trimester III Group II was much more complicated than that of women in Group I (Table. 3). So the women of Group II-threatening preterm delivery (t = 3.24; RR 1.971 [1.395-2.783]; NNT = 4.545; Se 0.663; Sp 0.583) were significantly more likely identified prematurity (t = 3.31; RR 4.833 [2.067-11.302] ; NNT = 5.522; Se 0.829; Sp 0.543), mild preeclampsia (t = 2.42; RR 2.333 [1.332-4.089]; NNT = 7.5; Se 0.7; Sp 0.54). Only Group II women diagnosed with severe preeclampsia, premature abruption of normally situated placenta, placental abnormalities. Note that only 11% of women of the Group II clinical had signs of placental anomalies in 7% of women placenta accreta, from 1% - increta placenta, placenta from 2 percreta. Noteworthy is the fact that in all cases of abnormally invasive placenta conception occurred in the first 3 months after myomectomy. Ultrasound signs of chronic disease were observed in the absolute number of women of the Group II, and 86% of women in Group I.

In assessing the clinical course of uterine fibroids during pregnancy ensuing we found that only the women in Group II was an increase in the number (from 3-5 to 7 knots) and / or the size of fibroid nodes (with d = 13-15 mm to d = 38 mm) (tab. 4). Do uterine fibroids during pregnancy increase was due to an increase in progesterone levels (endogenous and exogenous), this study can not be answered unequivocally. This requires additional definition progesterone receptivity of the fibroid nodes.

To estimate integrity of the scar after myomectomy using ultrasound presented great difficulties. During III trimester of pregnancy only 3% of women in the Group II at US examination in the anterior wall of the myometrium determined dashes of hyperechogenicity, local thin-

Table 1

Complications in the I trimester of pregnancy

Complications of pregnancy	Preconception treatment t (n=150)		No preconception treatment (n=150)	
	n	%	n	%
Threatened miscarriage	52	35	90	60*
The duration of hospitalization, bed-days	10 (6-15)		15 (9-25)	
Partial abruption of chorionic	20	13	15	10
Anemia	18	12	21	14

*** - p<0,001

Table 2

Complications in the II trimester of pregnancy

Complications of pregnancy	Preconception treatment t (n=150)		No preconception treatment (n=150)	
	n	%	n	%
Threatened miscarriage	22	17	66	44***
The duration of hospitalization, bed-days	11 (10-12)		16 (0-25)	
Partial abruption of chorionic	8	5	10	7
Anemia	no	0	3	2

*** - p<0,001

Table 3

Complications in the III trimester of pregnancy

Complications of pregnancy	Preconception treatment t (n=150)		No preconception treatment (n=150)	
	n	%	n	%
Threatening premature labor	34	22	67	45*
Preterm labor	6	4	29	19*
Preeclampsia	15	10	35	23**
mild	15	10	33	22
severe	нет	0	2	1
Chronic placental insufficiency	129	86	150	100
Abruption of placenta	нет	0	7	5
Предлежащие плаценты	нет	0	15	10
Abnormally invasive placenta (histologically)	нет	0	8	5
Abnormally invasive placenta	нет	0	16	11
(according to US only)			11	7
placenta increta			2	2
placenta percreta			3	2

*- p<0,05;** - p<0,01

ning of the myometrium 1-2 mm in diameter up to 30 mm, which is regarded as a failure of the uterine scar after myomectomy . Indeed, at laparotomy for the purpose of delivery by cesarean section was visualized thinning the uterus of land in the form of "niche" to 1-2 mm thick. When choosing delivery method in women in both Groups were taken into account absolute and relative obstetric indications. Given the myomectomy in women in the history of vaginal delivery path, pose a significant risk, and in the Group II were carried out much less frequently (p< 0,01) (tab. 5).

Therefore, in the presence of protocol operations with reference to the small remote node size, lack of opening of the uterus and uncomplicated postoperative course with myomectomy, the absence of ultrasonic signs of insolvency of the scar on the uterus, the length of the interval from the myomectomy before pregnancy for at least 1 year, deliveries were conservatively with constant control of the contractile activity of the myometrium (tocography) and cardiorhythmography of the fetus.

In caesarean section the thinning of the myometrium in the supposed myomectomy was visualized in 15% of women in the Group I and 20% of women of the Group II, and the localization of deformation myometrium scar on the back wall was only 5% of women in the Group I and 8% of women of the Group II. Thus, the feasibility of delivery by caesarean section only on the basis of the scar on the uterus after myomectomy most women can be treated as a subject of discussion. However, the lack of reliable non-invasive techniques, allowing guaranteed to exclude the failure of the uterine scar after cesarean section during pregnancy causes the clinician to refer such labor to a high risk for uterine rupture, fetal death, bleeding. In 59% of women in the Group I and 63% of women in the Group II myomectomy was performed during cesarean section.

In assessing the duration of labor in women in the Group I (n = 35) and the Group II (n = 12) significant differences were found: 8.6 (7-11) and 8.8 hours (8-11) hours, respectively. A similar assessment was in calculating the duration of cesarean section in women in the Group I (n = 115) - 71.4 (45-120) min. and the Group II women (n = 138) - 69 (50-100) min.

In the study of the flow of complicated childbirth it deserves attention is the fact that only 2 women the Group II-threatening uterine rupture was diagnosed in a timely manner. According to complications such as weakness or discoordination labor, both Groups were comparable.

In assessing blood loss during delivery notes that massive blood loss of more than 20 ml / kg was only 2% in women of the Group II, which was caused by an abnormality of the placenta attachment (placents percreta) (tab. 6). In other cases, blood loss in the number and urgency of women in both Groups were comparable. The cause of bleeding in the Group II 5% of women had PONRP, 10% - placenta previa, 11% - placental abnormalities. In other observations causes uterine bleeding were hypotension, and a combination of factors.

Conclusion. Uterine fibroids in reproductive period remains relevant for obstetricians and gynecologists. There are still many unresolved issues in the choice of anti-recurrence therapy of the uterine fibroid, quick access when myomectomy, the need to improve endoscopic extracorporeal knots, perfection of the qualification surgical team especially for women planning pregnancy. Obvious need to preserve women's reproductive health,

prevention of gynecological pathology, disciplined attitude to women prescribed therapy

To date, it remains relevant problem of effective recovery of reproductive function, of preconception preparation, prevention of complications of gestation in women with uterine fibroid and infertility associated with it. Obvious need to improve the system of measures aimed at improving the outcomes of pregnancy and childbirth for mother and fetus in women with uterine fibroid.

Table 4

Dynamics of growth of of myoma nodes in pregnancy

Complications of pregnancy	Preconception treatment t (n=150)		No preconception treatment (n=150)	
	%	n	%	n
Increasing the number of uterine fibroids	18	12	30	20
Secondary changes of myoma nodes (clinically)	8	5	16	11
Secondary changes of myoma nodes (according to US only)	7	5	10	7

** - p<0,01

Table 5

Methods of delivery

Method of delivery	Preconception treatment t (n=150)		No preconception treatment (n=150)	
	n	%	n	%
Vaginal	35	23	12	8* t=2.88
Cesarean section	115	77	138	92
Myomectomy during cesarean section	89	59	95	63

** - p<0,01

Table 6

Blood loss at delivery

The volume of blood loss ml/kg body weight	Preconception treatment t (n=150)		No preconception treatment (n=150)	
	n	%	n	%
5	7	5	9	6
5 – 8	40	27	32	21
8 – 10	47	31	44	30
10 – 15	54	36	60	40
15 – 20	2	1	2	1
Более 20	0	0	3	2

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