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The Outcomes of Different Organ-Preserving Treatment of Uterine Fibroids

ABSTRACT

The article reports a prospective study of women with uterine fibroids. The patients went to the clinic for conservative myomectomy and uterine artery embolization. Endovascular UAE has proved to be the most effective method of UF treatment, having fibroid nodes in the size up to 10 cm with a good vascularization, as well as submucous nodes localization. Thus, UAE among patients with UF provides little traumatic intervention with good clinical effect and reduction in the size of the uterus, as well as preserves the uterus, which is especially important for women with unrealized reproductive function, having contraindications to surgery and categorical rejection of it.

In this way, the optimal outcome of organ-saving UF treatment is achieved not only due to the skill of the surgeon, the adequacy of the selected surgical approach, providing minimization of operational risks, but also due to a whole complex of measures, including diagnosing disorders in various links of reproductive system and rational management of pre- and post-operative stages in accordance with complex rehabilitation.

Keywords: uterine myoma, uterine artery embolization, ccomplex postoperative rehabilitation.

INTRODUCTION

The realities of modern reproductive surgery show that even taking into account all variety of treatment technologies, debates about the question of expediency, selection criteria, indications, contraindications, long-term results of treatment of hyperplastic diseases of the uterus are still going on to clarify the preferred embodiment of a particular intervention. The revision of priorities in favour of organ reconstructive plastic surgery can be explained by rejuvenation contingent of women with uterine myoma who are interested in saving their reproductive function but often have large or atypical arrangement of fibroids [1,2].

Efficiency of uterine fibroids (UF) treatment technologies is the most debated subject of scientific research. Not only the pace of the reduction of the amount of fibroids and clinical symptoms, but also the rate of complications and recurrence of myoma growth are subject to comparative analysis. Despite the ambiguity of the results of different interventions – laparotomic myomectomy, endoscopy and endovascular – it is obvious that the focus of efforts

must be to improve not only the manual skills, but also the scope of rehabilitation of patients' life quality. Putting endovideosurgical operations into practice determined trendiness of laparoscopic approach in treatment of reproductive-age women with uterine myoma – due to its high levels of efficiency and minimum risk of complications. However, the idea of laparoscopic myomectomy priority has changed with the appearance of reports about uterine rupture in the place of a scar during the process of giving birth (1%) [3], which indicated the need for a differentiated choice of surgical access. Stratification of laparoscopic surgery in complexity, with the release of high-risk category in multiple uterine fibroids, large tumor size, especially interstitial, proves it justifiable to make "energy-consuming" operations in subserous nodes on the stem or shallow wide basis.

Interventional radiology advances contributed to the effective implementation of routine practice in the treatment of UF uterine artery embolization (UAE). Result of its use convince us in practicing this alternative method when having technical complexity of the conservative myomectomy or unjustifiably high risk of trauma using other way of access[9].

Optimization of the quality of life of patients with UF requires not only the analysis of productive using of saving surgery opportunities, but recovery from operational stress [6]. Results of the analysis of quality of life (QOL) of women after treatment of UF using various rating scales: Nottingham Health Profile (NHP), Medical Outcomes Study Short Form-36 (MOS SF-36), Uterine Fibroid Symptom and Quality of Life questionnaire (UFS-QOL) are variable, which can be explained by the difference of samples, lack of post-operative rehabilitation or inadequate capacity [6].

The proof for the effectiveness of uterine artery embolization (UAE) in treatment of symptomatic uterine fibroids can be the data by AJ Smeets et al. (2012) [4] about the reduction of clinical manifestations of the disease among 70.6% of women 46 months later after endovascular impact, based on the results of the standardized questionnaire UFS-QOL. There are reports about long-term sustainable improvement in quality of life with a slight relapse – 6 years after the UAE at 17% [8]. Despite the advantage of non-invasive treatments for UF in comparison with hysterectomy [5], after the processing of personal data on the scale of UFS-QOL there were best indicators of quality of life after hysterectomy, despite the considerable relief among patients 12 months after different treatment options [7].

Considering ambiguity of the data on the improvement of quality of life after various options of sparing technologies, analysis of the reduction rate of the amount of fibroids and the

reduction of symptoms of UF is required to predict benefits of choosing options for intervention. The chance of reducing postoperative complications and recurrence of the disease is possible after the optimization of different approaches, adequate selection of UF treatment technologies, rational preoperative preparation and recreational activities after the intervention. The lack of evidence proving efficiency of the above-mentioned tactics defines the goal aimed at comparative analysis of the quality of life of women after different UF treatment technologies and outcomes of the disease, depending on the availability of rehabilitation.

MATERIALS AND METHODS

To achieve the goal a prospective study of 675 women with uterine fibroids was carried out. These patients went to the clinic for conservative myomectomy and uterine artery embolization. Depending on the technology of treatment and the presence of postoperative rehabilitation, entire contingent of women with uterine fibroids was divided into groups: I – after laparotomic myomectomy (LTM) ((n = 216) and after complex rehabilitation (CR), II – after LTM and without CR (n = 51), III – after laparoscopic myomectomy (LSM) and CR (n = 248), IV – after LSM and without CR (n = 36), V group – after UAE and CR (n = 108) , VI group – after UAE without CR (n = 26).

Comprehensive pre-operative examination included Doppler ultrasound, hysteroscopy, histological examination of scrapings of the endometrium, treatment of persistent chronic inflammatory diseases of genitals. Antimicrobial therapy was provided if needed (in cases of exacerbation of chronic inflammation of the genitals with the release of infectum in diagnostically significant titer). Complex rehabilitation after the intervention included prevention of adhesions (3000 IU Longidaza suppositories or intramuscular №10), immunocorrection (depending on the nature of the violation of non-specific resistance there were used endogenous interferon inducers №10, UFO autologous №7-10), antioxidants (tocopherol acetate 200 mg every day for a month), disaggregates (Curantyl 75 mg 2 times a day for 3 weeks), the restoration of genitals eubiosis (Gynoflor E, Normoflorin, Primadofilus).

To prevent recurrence of fibroids growth the following medicaments were prescribed in accordance with hormone-related diseases and interest in the subsequent implementation of the reproductive function: a GnRH agonist (Zoladex), intrauterine Levonorgoestrelum-releasing depot system "Mirena", low-dose hormonal contraceptives (Regulon, Jeanine).

UAE was carried out by the standard technique, with preliminary angiography research, units' sonography, Doppler; polyvinylalcohol (PVA) particles measuring between 350 and 900 or

hydrogel (AAA Co., Russia) were used as emboli. UAE was made when having contraindications to other organ-preserving treatment options or their inefficiency (hormone), nodes greater than 10 cm in diameter.

The treatment results were evaluated by the subjective self-esteem of women, patients' questioning about the dynamics of symptoms, menstrual cycle, the quality of life at baseline and 3, 6, 12 months after the treatment, as well as by ultrasound evidence and magnetic resonance imaging. Quality of life assessment was performed using a questionnaire before surgery (LTM, LSM, UAE) and after 3 and 6 months, according to the modified American Association of Obstetricians and Gynecologists Quality of Life Questionnaire UFS - QOL among patients with UF.

The duration of patients' observation and follow-up after the surgery was 12 months.

Statistical analysis of the data was performed using the statistical application package «Statistica for Windows» v. 6.0, Stat Soft Inc (USA). Descriptive statistics, criterion χ^2, Student's t test (t) for unrelated groups were used for the description of the indicators presented in the form of quantitative variables. Statistically correct was the factor, the significance level of which is less than 0.05 ($p < 0.05$).

RESULTS AND DISCUSSION

The results of the survey of patients 6 months after various UF treatment technologies showed mostly accurate reduction of negative symptoms, including prolonged and heavy menstruation, chronic glandular deficiency anemia, feeling of heaviness in the abdomen, violation of adjacent organs, being reflected in the decrease in the quality of life and the limit of working ability. The severity of clinical manifestations after UAE in groups with complex rehabilitation and without it was still different.

In general, the study of quality of life among patients after various treatment technologies correlated with minimizing the symptoms of dysmenorrhea and dyspareunia, disappearance of pelvic organs compression signs, reduction of menstrual blood loss, which prevailed in groups after complex rehabilitation course. Normalization of hematological parameters occurred 3 months after monitoring all patients with anemia caused by meno- and menometrorrhagia.

UAE efficiency in removing menometrorrhagia during the year was 92.5%, which can be regarded as a fairly high rate. Among 22 patients with symptoms of compression of adjacent organs (the heaviness in the abdomen, dysuria, constipation) leveling of symptoms was observed in 95.5%. 86.6% of women had regular menstrual cycle, amenorrhea developed among 13.4% of women 6 months later.

Normalization of hemoglobin by 12 months' time occurred in 46.1% - 76.9% cases with complex rehabilitation compared to 80.5– 91.7% without CR.

The criterion for the effectiveness of treatment techniques was considered significant reduction in severity of the condition index 6 months after compared to baseline: 50.7% after UAE ($p < 0,05$), 44.2% on average – after LSM and LTM, in the absence of rehabilitation – 36.7% on average.

Increasing the integral index of quality of life after the intervention took place due to the relief of symptoms and almost leveling of negative emotional reactions to the settings on the readiness to regular uterine bleeding and risk of endometrial malignancy.

Clinical benefit in the form of regression of symptoms and downsizing nodes was marked in most cases (up to 81.3%) after embolization of uterine fibroids. Dynamics of volume reduction of dominant subserous and subserous-interstitial nodes 3 months after was 42% in the group with CR, uterus – 45%, 6 months after – 57.8% and 65.4% respectively. Full devascularization of dominant myoma node (90%) one month after the UAE was observed among 83.6% of women at 95.5% after 3 months, 93.3% - after 6 months; with multiple nodes – among 60.4% of women. Intraoperative-pain syndrome of varying severity accompanied all parts of UAE, the combination of it with the blood leucocytosis was observed among 13 women. This condition was not regarded as a side effect or complication, it was interpreted as a manifestation of metabolic adjustment accompanied by myoma node tissue degradation, the consequences of which were not considered within adequate tactics of postembolizational period. The result of UAE together with submucous nodes or centripetal growth reveals in reducing their size more than doubled and expulsion of the uterine cavity (1-6 months after UAE), which was accompanied by an increase in menstrual blood loss and caused menorrhagia and metrorrhagia.

Spontaneous nodes expulsion that required hysteroresectoscopy took place in 15 cases. Hysteroscopic removal of fibroid necrotic mass at 8% was complicated by the development of acute endometritis treated conservatively (anti-bacterial, anti-inflammatory, detoxification therapy) in two patients. In one case, against the background of acute painful endometritis due to submucous node migration into the uterus 2 weeks after embolization, supravaginal amputation of the uterus was made, without appendages. 2 patients had a hysterectomy without appendages because of large growing node symptoms. Bleeding as UAE complication in the submucous uterine myoma was observed in two cases 3 months after the intervention, one – in 11 months and demanded hysterectomy without appendages.

Detailization of postoperative complaints showed gradual disappearance of pain and discomfort that occurred among the vast majority (96%) of women before the treatment: during 3 months after UAE – 26.1%, 6 months – 11.9%, a year – 8.9%. Still preserving moderate pain 3-4 months after UAE combined with node units reduction on average of 30-40% (n = 24) was observed mainly in the absence of a rehabilitation course, which determined a minor downward trend of QOL scales. After UAE in terms from a month to a year 26 patients were operated on (in addition, 5 – with the expulsion of nodes), from them, 6 – because of the absence of clinical effect, 10 – because of the progressive myoma growth. In the absence of clinical effect (n = 9) (among 6 patients without a rehabilitation course) 3 months after UAE LTM was performed in cases of four women (with two of them having adenomyosis of the III degree), 4 months – in cases of five women (with adenomyosis II and III having two and one of them, respectively). Additional coagulation of endometriosis, followed by prescribing GnRH agonists (GL), was required in one of the episodes. Short-term and small (on average, 20% of the original) amount of the node units reduction preceded preserving of symptoms and further nodes growth. Revascularization episodes occurred in cases of 19 women, which was the basis for hysteroresectoscopy 2 months after in cases of three women, LSM – two women, LSM and coagulation of endometriosis 4 months after in cases of two patients, repeated endovascular intervention – four patients. In one case, LTM coagulation of endometriosis was preceded by separate diagnostic curettage of the endometrium. A year after the UAE (node units decrease by 25% 6 months after turned to growth and revascularization) two patients needed radiotherapy without appendages, in one case gonadotropin supplementation has been effective.

In assessing the parameters of quality of life 3 months after UAE the highest regression of symptoms was determined in combination with CR, that was realized in positive dynamics of such parameters as "uneasiness decrease", "alertness / fatigability," "self-image" and "sexual function". 6 months later after various interventions UAE effectiveness was confirmed by statistically significant improvement in a number of increased parameters: "alertness / fatigability" (by 53,7%) ($p < 0,05$) – by one and a half times in contrast to LSM and LTM (on average , 37.5%); "Self-image" (by 62.2%) – by 1.2 times in comparison with the indicator for LSM, by 1.7 times – for LTM ($p < 0.05$); "Sexual function" (by 56.2%) – by 1.5 and 1.8 times ($p < 0.05$), respectively. Regardless of the type of intervention, the growth of "activity" parameter appeared to be comparably high – by 46.1% on average (with the CR after UAE – by 32% compared to its absence ($p < 0.05$), after LSM and LTM – by 17 1% on average), "control" – by 44.6% on average.

The morphology of endometrial samples before the operation turned out to be mosaic: glandular endometrial hyperplasia – among 133 women with UF, glandular fibrous endometrial polyp – among 149, ferruginous – among 75.

The frequency of separate diagnostic curettage of the endometrium after UAE in connection with endometrial hyperplasia prevailed when combined UF with adenomyosis – 5.7% with CR and a quarter in its absence ($p < 0.05$).

Identification of atypical endometrial hyperplasia (AEH) as well as focal hyperplasia with adenomatosis determined without the need for hysterectomy of the uterus, in both cases among patients without CR. The greatest number of UAE complications (n = 4) was revealed within submucous UF and caused hysterectomies without appendages (n = 3) and one supravaginal uterus amputation without appendages. Relatively slight and temporary reduction in the scales of quality of life within symptomatic UF and its combination with adenomyosis without CR after the operation was the reason for LTM among 4 patients, LSM among 4 patients; supravaginal uterus amputation without appendages among 4 women, repeated UAE among 4 women; the absence of clinical effect caused LTM among 9 patients.

In order to prevent recurrence of the disease more than a third of women after conserving surgery received hormone therapy by agonists of gonadotropin-releasing hormone for 4-6 months (Zoladex, Diferelin), with the restoration of the menstrual cycle on average within 28 days after their cancellation. The above-mentioned tactics has identified the reduction of menstrual blood loss and the relief of dysmenorrhea severity and frequency. In total, relapse during the observational follow-up was noted among 74.5% patients after LTM, 69.4% – after LSM, 73.1% – after UAE, mainly because of CR absence after the operation.

CONCLUSION

Taking into consideration the ambiguity of long-term UAE results, we have to provide details of the possible causes of nodes relapse, paying respect to pathogenetic aspects. Thus, despite the episodes of relapse, the causes of which we have to clarify, UAE presents a highly effective organ-saving treatment of uterine fibroids among women of fertile age planning pregnancy. It is also an alternative to radical hysterectomy among premenopausal women with multiple nodes.

In this way, the optimal outcome of organ-saving UF treatment is achieved not only due to the skill of the surgeon, the adequacy of the selected surgical approach, providing minimization of operational risks, but also due to a whole complex of measures, including

diagnosing disorders in various links of reproductive system and rational management of pre- and post-operative stages in accordance with complex rehabilitation.

References

1. Gur'eva V.A. Karpenko A.A. Borisova O.G. Mesto ehmbolizatsii matochnykh arterij v terapii miom matki [Place of uterine artery embolization in uterine fibroids treatment] Roscijskij vestnik akusherstva i ginekologii [Russian journal of Obstetrics and Gynecology]. 2008, No 2, pp. 40 - 44.
2. Davydov A.I. Pankratov V.V. Yagudaeva I.P. Vosstanovitel'noe lechenie posle organosberegayushhikh operatsij u bol'nykh podslizistoj miomoj matki i adenomiozom [Medical rehabilitation after organ-preserving surgery among patients with organ-submucosal uterine fibroids and adenomyosis]. Voprosy ginekologii, akusherstva i perinatologii [Issues of gynecology, obstetrics and perinatology]. 2011, No 10 (6), pp.13 - 21.
3. Savel'eva G.M. Kurtser M.A. BreusenkoV.G. Endoskopicheskaya miomehktomiya: za i protiv[Endoscopic miomektomya: pros and cons]. Voprosy akusherstva, ginekologii i perinatologii [Questions of obstetrics, gynecology and perinatology]. 2007, V. 6, No 1, pp. 57-60.
4. Long–term follow–up of uterine artery embolization for symptomatic adenomyosis / A.J. Smeets, R.J. Nijenhuis, P.F. Boekkooi [et al.] // Cardiovasc Intervent Radiol. – 2012. – V.35. – N4. – P. 815 – 824.
5. The effect of uterine fibroid embolization on lower urinary tract symptoms / D. Shveiky, C.B. Iglesia, D.D. Antosh [et al.] // Int Urogynecol J. – 2013. – V.24. – N 8. – P.1341–1346.
6. The responsiveness of the uterine fibroid symptom and health–related quality of life questionnaire (UFS–QOL) / G. Harding, K.S. Coyne, C.L. Thompson [et al.] // Health Qual Life Outcomes. – 2008. – V.12. – N 6. – 99 p.
7. Uterine artery embolization for symptomatic uterine fibroids / J.K. Gupta, A. Sinha, M.A. Lumsden [et al.] // Cochrane Database Syst Rev. – 2012. – V.16. – N 5. – CD005073.
8. Validation of the UFS–QOL–hysterectomy questionnaire: modifying an existing measure for comparative effectiveness research / K.S. Coyne, M.K. Margolis, J. Murphy [et al.] // Value Health. – 2012. – V.15. – N5. – P. 674–683.

9. Van der Kooij S.M. Review of nonsurgical/minimally invasive treatments for uterine fibroids / S.M. Van der Kooij, W.M. Ankum, W.J. Hehenkamp // Curr Opin Obstet Gynecol. – 2012. – V.24. – N 6. – P. 368 – 460.

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