Hysteromyoma is the most common disease of the female reproductive system. The frequency of this pathology is between 25 and 50% in women of the reproductive age (1). The problem of fertility preservation in patients with uterine myoma is of particular importance, given, on the one hand, "rejuvenation" of the disease, on the other – abilities of the modern reproduction therapy and expansion of reproductive period boundaries. Currently, hysteromyoma is diagnosed in 12.5% of pregnant (2, 3), and in 18-24% of women is the only etiologic factor of infertility (4). These trends cause an increased interest in minimally invasive organ-saving methods of hysteromyoma treatment, such as uterine arteries (EUA) embolization, which allows saving childbirth functions and restoring impaired reproductive function in female patients of childbearing age.

Despite the large number of domestic and foreign publications on the effectiveness and safety of EUA as a method of hysteromyoma treatment (5-7), a number of problems associated with its remote results, and primarily the impact on fertility, the course and outcomes of pregnancy are still unsolved. Currently, there are no large randomized studies on the clinical course of pregnancy after EUA. Most articles lack information about hysteromyoma characteristics, methods of previous treatment, initial fertile status of female patients, which probably explains a large variety of results. Until recently, myomectomy was considered to be the "gold standard" of myoma treatment for women who did not realize reproductive function, while EUA was not recommended for women interested in childbirth.

Thus, to date there is no clear answer about the method of selection of interstitial hysteromyoma treatment for patients who are interested in maintaining fer-

**Summary:**

The course and outcomes of pregnancy in patients with hysteromyoma in different treatment methods.

**V.A. Gurjeva, O.V. Kolyado, Y.O. Karacheva**

The need to study the effect of uterine arteries (EUA) embolization on fertility is due to the fact that the reproductive behavior of a modern woman supposes planning to become pregnant after the age of 30 and older, when hysteromyoma is observed in every 4 women. This fact requires a search for the best types of organ-saving myoma treatment, with a guarantee of consecutive pregnancy and childbirth. The aim of the study was to compare the course and outcome of pregnancy in women with hysteromyoma after EUA and myomectomy to determine the choice of the most optimal treatment method in women with unrealized motherhood. The course and outcomes of pregnancy and condition of newborns of 147 patients were studied: after EUA (main group) and after myomectomy (comparison group 1), as well as patients with intact myomas (comparison group 2), and women without hysteromyoma (comparison group 3). The material was accumulated retrospectively by examining the medical documentation: medical records, notification cards of pregnant and maternity women, birth records and records of infant development. It was found that women treated by myomectomy and EUA had differences in the nature of complications during pregnancy, the course of puerperal period, method of delivery. The risks for subsequent pregnancies were more real in patients after myomectomy due to myoma recurrence in 50% of cases during pregnancy, scars on the uterus (after myomectomy and cesarean). No new knots, growth and vascularization of the existing myoma were observed after EUA, which makes it possible to regard EUA as the method of choice, especially in cases of motherhood not finally realized.

**Key Words:** Hysteromyoma - Fertility - Embolization of uterine arteries - Myomectomy - Pregnancy outcomes.
tuality, and there are a few studies comparing these two methods in terms of the course and outcomes of pregnancy.

**Materials and methods**

144 women of reproductive age were examined. The material was accumulated retrospectively by analysis of the medical documentation: medical records, notification cards of pregnant and maternity women, birth records and records of infant development. The main group (n=32) included women of reproductive age with hystroomyoma treated by EUA. Embolization of uterine arteries was performed on the clinical base of the department of Obstetrics and Gynecology in the X-ray operating theater of the Regional State Budgetary Health Care Facility “Regional Clinical Hospital”. First, puncture of the right or left femoral artery was performed, then an introducer of 6 or 7 French (Fr) in diameter was inserted through the wire system into the artery. After that a specially modified catheter was introduced into the femoral artery following Seldinger’s technique for alternate catheterization of the common iliac (CIA), and then internal iliac artery (IIA) on the right and left. After IIA pool angiography and visualization of the uterine mouth artery, according to the captured image, using “Road map” feature, super selective uterine artery catheterization was performed using a hydrophilic conductor and angiographic catheter with a diameter of 4-5 Fr. Uterine artery catheterization was followed by Urografin or Ultravist angiography with the contrast injection rate of 1 ml/sec., volume of 4-6 ml. At the same time frame-by-frame exposure was performed at a rate of 2-4 frames per second, starting with the arterial and ending with parenchymal opacification phase (the diameter of uterine arteries, contrasted sizes of myomatous knots and the nature of artery architecture in knots were evaluated to avoid atypia, and connection in the ovarian arterial system, topographical ratio of the blood flow in the ovarian branch of uterine artery and nodular blood flow).

Then, the inner end of the catheter was moved maximally distantly until the effect of its “wedging” in the artery lumen. Then, the embolic agent was introduced into the cathether [TruFill™ (Johnson & Johnson) with microparticle size of 500-700 N/m.c] with the repeated control angiography in the former mode. The result of the surgery was evaluated by a complete cessation of arterial blood flow in myomatous nodes. The system of the catheter and the introducer was removed, and hemostasis of the punctured site was performed. The aseptic bandage was applied. The 1-st control group included women with a history of myomectomy (n=32) and post-operative period of not less than 2 years. Myomectomy was performed in the Gynecological Department of the Regional State Budgetary Health Care Facility “Regional Clinical Hospital” via laparotomy access, with suturing of the node bed after myomectomy. All surgical interventions (in the main group and in the comparison group No. 1) had no complications.

Given that the presence of hysteromyoma as such can cause complications during pregnancy and childbirth, the third comparison group, including women with interstitial myoma, with hysteromyoma not surgically treated previously (n=40), was formed to assess the impact of the above factors. The control comparison group (the fourth) involved women without hysteromyoma.

All women had interstitial location of nodes, only one patient had a submucosal myoma of the uterus (in the main group).

The mean volume of the dominant node in patients of the main group amounted to EUA – 111.8±34 cm³. EUA was effective in 30 patients (93.8%). In 2 (6.3%) patients due to incomplete blood flow blockade, blood supply of the node restored in 1 and 2 years after embolization with resumption of tumor growth (relapse). Subsequently, one of them was subjected to repeated EUA with a full effect, the second woman refused from further treatment.

By the time of pregnancy, all women of the main group showed a pronounced decrease in the average size of the dominant node to 53±15 cm³. The patient with submucous hysteromyoma had myolysis of the node after EUA that fully restored the uterus architecture.

Patients with interstitial localization of the nodes 67.6±14 cm³ in size made the second group, and those with 94±7 cm³ – the third.

Patients in comparison groups were randomized by age, social status, and place of residence. The following indicators were used as evaluation criteria of therapy methods in the main and the first comparison group: pregnancy after surgery (EUA, myomectomy), frequency and nature of the complications of pregnancy and childbirth, the course of post-partum period, pregnancy outcomes (condition of newborns), recurrence of hysteromyoma in pregnancy.

Statistical analysis of the data obtained was performed using Statistica 10 software package. Quantitative values are presented as mean ± standard deviation. Student’s t-test was used for comparison of quantitative data attributes. Quality data attributes were compared using contingency tables 2×2 by Pearson χ² criterion with Yates correction and using Fisher’s exact test. Differences were regarded as statistically significant at p<0.05.

**Results**

The average age of women in the main group was 34.2±3.2 years, and did not differ from the age of wo-
The course and outcomes of pregnancy in patients with hysteromyoma in different treatment methods

Table 1 - Frequency of extragenital pathology in patients.

<table>
<thead>
<tr>
<th></th>
<th>Main group (n=32)</th>
<th>1 comparison group (n=35)</th>
<th>2 comparison group (n=40)</th>
<th>3 comparison group (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular diseases</td>
<td>15 46.8</td>
<td>16 45.7</td>
<td>18 45.0</td>
<td>20 50.0</td>
</tr>
<tr>
<td>Endocrine pathology</td>
<td>6 18.8</td>
<td>7 20.0</td>
<td>9 22.5</td>
<td>8 20.0</td>
</tr>
<tr>
<td>Gastrointestinal diseases</td>
<td>4 12.5</td>
<td>4 11.4</td>
<td>4 10.0</td>
<td>5 12.5</td>
</tr>
<tr>
<td>Urinary system diseases</td>
<td>2 6.3</td>
<td>3 8.6</td>
<td>3 7.5</td>
<td>3 7.5</td>
</tr>
</tbody>
</table>

All pregnant women were on file in the dispensary at the place of residence and were fully examined in accordance with the applicable care procedure.

The patients had somatic burdened history that probably was due to the age factor. The structure of extragenital pathology was dominated by cardiovascular system diseases, observed in almost every second woman, and endocrine pathology (Table 1). Diseases of the gastrointestinal tract and urinary system were less common.

As the Table shows, the groups studied were comparable in terms of extragenital disease frequency. It is known that extragenital pathology significantly increases the probability of complicated pregnancy, being a risk factor for the development of placental insufficiency, threat of pregnancy termination and preeclampsia, however lack of differences allowed to assess the impact of EUA and myomectomy on pregnancy outcomes.

No differences in the obstetric history of women in the comparison groups were observed (p>0.05). As can be seen from Table 2 most of the patients had burdened obstetric history. Thus, almost one in five had cases of miscarriage, 6-8% of patients was infertile. It should be noted that after EUA fertility was restored in all patients of the main group with infertility. Pregnancy occurred without the use of auxiliary reproductive technologies. After myomectomy, fertility was restored in one patient, in two other patients pregnancy was the result of ART (in one case infertility was associated with tubal-peritoneal factor, in the second – infertility genesis was unclear).

In general, patients of the main group after EUA had the same volume of hysteromyoma (53±15 cm³), as women of the third group (47±9 cm³), but the original node size in the main group was 2.3 times larger (111.8±34 cm³). The regression after EUA procedure was accompanied by a zone of aseptic necrosis with uterus tissue fibrosis and endo- and myometrium functional viability disturbance. Therefore, at equal node size, the conditions for carrying of pregnancy were different. Uterine trauma after removing a node in women of the first comparison group also influenced myometrium function, but endometrium state was not affected in this case. So it is quite understandable that if pregnancy occurred in women of the main group, the increased frequency of pathological placentation in the first trimester, observed in 44% patients, was due to endometrium functional disability after EUA (Figure 1). In 12.5% of patients placentation anomalies persisted up to full term of gestation, and there were such severe forms of this pathology as the placenta ingrowth (1 case) and central placenta previa (2 cases).

No differences in terms in frequency of the threat of

Table 2 - Obstetric history of the patients.

<table>
<thead>
<tr>
<th></th>
<th>Main group (n=32)</th>
<th>1 comparison group (n=35)</th>
<th>2 comparison group (n=40)</th>
<th>3 comparison group (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Natural childbirth</td>
<td>10 31,3</td>
<td>13 37,1</td>
<td>14 35,0</td>
<td>13 32,5</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>3 9,4</td>
<td>3 8,6</td>
<td>4 10,0</td>
<td>5 12,5</td>
</tr>
<tr>
<td>Induced abortion</td>
<td>8 25,0</td>
<td>9 25,7</td>
<td>11 27,5</td>
<td>10 25</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>6 18,8</td>
<td>7 20,0</td>
<td>7 17,5</td>
<td>8 20,0</td>
</tr>
<tr>
<td>Infertility</td>
<td>2 6,25</td>
<td>3 8,5</td>
<td>3 7,5</td>
<td>3 7,5</td>
</tr>
</tbody>
</table>
premature birth in the third trimester, delay in fetal development and preeclampsia were observed between the groups (Table 3).

The frequency of premature births in the main group was 6.3%, in the first comparison group – 5.7%, in the second comparison group – 7.5 and 5.0% in the control group (p>0.05). However, their causes were different. In the main group, the preterm urgent delivery by Caesarean section was caused by bleeding due to placenta previa (6.3% - 2 patients). In other groups preterm delivery was due to the discharge of amniotic fluid and cervical incompetence.

It should be noted that EUA did not increase the incidence of abdominal delivery. In 53% of cases delivery was vaginal, that did not exceed this value in patients of the 2nd and 3rd comparison groups. At the same time 94.3% of women gave birth in abdominal way (p <0.05) after myomectomy. The main indications for operative delivery were combination of uterine scar and burdened obstetric history. Three patients in this group were refused from Caesarean section. Two of them gave birth in a spontaneous way without complications; one pregnant was operated in the first period of childbirth on an emergency basis. Therefore, it was not possible to assess the course of spontaneous childbirth in women with myomectomy due to the fact that they mostly delivered in abdominal way. In three other groups there were no differences in the frequency of birth complications, thus it can be concluded that the contractile activity of the uterus was not affected after EUA (Table 4).

Obstetric hemorrhages in the study group were significantly more common: 15.6% of cases (5.7% in the first comparison group, 5% in the second and third groups), and in 80% of cases they were caused by placental pathology, and in 20% of cases - by hypotonic hemorrhage. In all other women of the comparison groups, the cause of postpartum hemorrhage was uterine hypotension, including after abdominal delivery in women with a history of myomectomy.

After myomectomy postpartum period was signifi-
cantly more commonly (in 14.7% of patients) complicated by uterine subinvolution (6.3% in the main group, 7.5% in the second comparison group, 10% in the third comparison group). The cause for uterine contractility failure in these patients was scars after myomectomy and cesarean section (Table 4).

Perinatal outcomes in comparison groups were similar: no asphyxia in newborns was observed, children in all comparison groups were born with APGAR scores of 8 points, rarer with 7 and 9 points (Table 5). The average weight of children in the study group was 3250±404 g, in women with a history of myomectomy – 3360±531 g, in the second comparison group, in women giving birth with uterine myoma – 3430±379 g, and in patients who did not have hysteromyoma – 3440±382 g. All children were discharged in satisfactory condition.

No recovery of hysteromyoma blood supply during pregnancy and nodes growth was observed in women after EUA. On the contrary, during cesarean small myomatous nodes of different locations were identified in almost every second patient with a history of myomectomy, i.e., relapse occurred in 50% of cases.

Table 4 - Frequency of complications during childbirth.

<table>
<thead>
<tr>
<th>Childbirth pathology</th>
<th>Main group (n=32)</th>
<th>1 comparison group (n=35)</th>
<th>2 comparison group (n=40)</th>
<th>3 comparison group (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>abs. %</td>
<td>abs. %</td>
<td>abs. %</td>
<td>abs. %</td>
</tr>
<tr>
<td>Premature discharge of amniotic fluid</td>
<td>6 18,8</td>
<td>-</td>
<td>7 17,5</td>
<td>8 20</td>
</tr>
<tr>
<td>Premature placental abruption</td>
<td>2 6,3</td>
<td>-</td>
<td>2 5</td>
<td>2 5</td>
</tr>
<tr>
<td>Anomalies of childbirth activity</td>
<td>3 9,4</td>
<td>1 3,5</td>
<td>5 12,5</td>
<td>3 7,5</td>
</tr>
<tr>
<td>Pathology of postpartum period</td>
<td>1 3,1</td>
<td>-</td>
<td>1 2,5</td>
<td>2 5</td>
</tr>
</tbody>
</table>

Table 5 - APGAR scale evaluation of full-term newborns.

<table>
<thead>
<tr>
<th>APGAR scale scores</th>
<th>Main group (n=30)</th>
<th>1 comparison group (n=33)</th>
<th>2 comparison group (n=37)</th>
<th>3 comparison group (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>abs. %</td>
<td>abs. %</td>
<td>abs. %</td>
<td>abs. %</td>
</tr>
<tr>
<td>Less than 7 points</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7 points</td>
<td>5 16,7</td>
<td>5 15,1</td>
<td>6 16,2</td>
<td>7 18,4</td>
</tr>
<tr>
<td>8 points</td>
<td>20 66,7</td>
<td>21 63,6</td>
<td>25 67,6</td>
<td>29 76,3</td>
</tr>
<tr>
<td>9 points</td>
<td>5 16,7</td>
<td>7 21,2</td>
<td>6 16,2</td>
<td>2 5,3</td>
</tr>
</tbody>
</table>

The course and outcomes of pregnancy in patients with hysteromyoma in different treatment methods

Increased number of patients of childbearing age, as well as reproductive disorders associated with such pathology as hysteromyoma is not only of a medical, but also a significant social problem. Despite the recent advances of pharmacotherapy, drug treatment of hysteromyoma is temporary in nature, whereby surgical treatment is still the main tactics to treat this disease (8, 9). In addition, use of organ-saving techniques such as myomectomy and embolization of uterine arteries is preferable in women interested in childbearing (10). Until recently American Society of Obstetricians and Gynecologists (ACOG) and the Society of Interventional Radiologists (SIR) recommended myomectomy as a method of treating patients planning pregnancy. Since there is no sufficient evidence for its safety, EUA was used in women of childbearing age only if myomectomy was technically difficult and was associated with a high risk of increasing the volume of intervention (11, 12). Assessment of the impact of various types of hysteromyoma surgical treatment on fertility is an urgent problem. Of course, it is necessary to consider that hysteromyoma can often be the independent cause of infertility and a risk factor of complicated pregnancy and delivery (3, 13). In addition, the majority of women needing surgical treatment are in late reproductive age, which also reduces the chances of pregnancy and its physiological gestation (14-16). In recent years, in Russia, as in many other countries EUA is becoming increasingly popular method of therapy, including cases of infertility due to myoma. This is primarily due to the data on the relief of the symptoms associated with myoma. Thus, there is an 85-94% decrease in menorrhagia, disappearance of the symptoms of dysfunction of the adjacent organs – by 60-96%, decrease of the uterus size (myomatous nodes) – by 35-60%, regression of pain syndrome in most patients (17-19). According to EUA register (FIBROID), 95%
of patients noted improvement in the quality of life in post-embolization period (7). ONTARIO research, realized in 2004, which included analysis of EUA555 cases, has established obvious effect of embolization on fertility recovery in 65% of women (19). The study carried out in 2011 in Lisbon (Portugal), has forced to reconsider the traditional attitude to myomectomy as to a “gold standard” of hysteromyoma treatment in women of childbearing age. The study contingent included women in whom myomectomy was not indicated due to technical complexity. Equal frequency of fertility restoration was observed in this paper: after EUA – in 58.1% of cases and after myomectomy – in 57% (20). However, there is no published data related to EUA course of pregnancy. So it is necessary to analyze the endomyometritis morphofunctional condition. This problem should be studied. At present there is no conclusive evidence both of pathogenesis of this complication and rehabilitation measures. It is also necessary to mention bleeding frequency in the main group due to placentation pathology that was more common – in 15.6% of cases.

The obtained results agree with those of the foreign Authors, e.g. increased frequency of obstetric hemorrhage in 22% due to placentation anomalies was noted by Pron et al. (21). The threat of pregnancy termination was observed in women after EUA and myomectomy with the same rate. Such pregnancy complications as preeclampsia, fetal growth retardation were also similar in comparison groups. The rate of premature births was the same in women after EUA, after myomectomy in women with and without hysteromyoma. The published data on the rate of premature births are quite contradictory. The study by Carpenter and Walker (2005) (24) and Pron et al. (2003) (21) showed higher rate of premature births after EUA compared with the general population (22 and 20%, respectively) (19, 22). On the contrary, this figure did not differ from the general population value in the meta-analysis performed by Mohan and Hamblin (25). As for the course of postnatal period, it was more often complicated by uterine subinvolution in patients after myomectomy, while EUA does not influence uterine contractile activity. Some Authors noted an increased frequency of caesarean section after EUA (23). However, in the present study, 53% of patients with hysteromyoma treated by EUA had vaginal birth, and this figure was not higher than in women from the 3rd control group and the comparison group. The frequency of abdominal delivery is almost 2 times higher in women after myomectomy (94.3%) (p<0.05). The main indication for their operative delivery was the combination of the uterine scar and burdened obstetric history. Thus, myomectomy risks are much higher compared to minimally invasive intervention – EUA, which does not require rehabilitation measures. Risks during operative delivery also were more marked in women who underwent myomectomy, as well as complications in the postnatal period, which were observed in this group, considering uterine scar and abdominal delivery. Perinatal outcomes were similar in all the groups. Different prognosis should be mentioned concerning the reproductive potential of the compared groups of women treated by EUA and myomectomy.

No fibroids, growth of the existing fibroids, increase in their vascularization was observed in women after EUA. On the contrary, in every second patient with a history of myomectomy small fibroids of different locations were found during cesarean section, i.e., there was a disease recurrence – in 50% of cases, and an obvious risk of growth of the emerging fibroids. An important argument in favor of EUA as a method of choice for women with hysteromyoma on the basis of our study is the fact that initially the patients at the stage of choosing a method of treatment were in the group with higher infertility risk and complicated course of pregnancy, due to various sizes of the histoma size. One of the reasons to justify the EUA method in women of the main group was a large myoma size – 111.8±34 cm³, which was 1.7 times higher (67.6±14 cm³) than the size of myomatous nodes in women who planned myomectomy, and 2.4 times higher (47±9 cm³) than in women who became pregnant spontaneously without planning pregnancy. After treatment, node size decreased by more than 2 times and was found to be similar to that in patients of the second group. But incidence of complications was more significant in women of the main group, that is primarily due to the initial histoma size and changes in end omyometritis morphostructure due to EUA, and namely the consequences of myomatous nodes infarction, aseptic necrosis on the background of blood flow arrest and further organization, hardening and fibrotization on the background of histoma regression. It is also necessary to take into account possible changes in myometrium as a consequence of temporary hypoperfusion due to EUA.

Conclusion

Thus, uterine arteries embolization can be regarded as the organ-saving method of hysteromyoma treatment, contributing to restoration of fertility in case of infertility caused by hysteromyoma. The rate of pregnancy complications and outcomes in case of more than 2 times larger hysteromyoma in women after EUA have no differences compared with patients after myomectomy. The nature of complications was different. Myomectomy performed at a lower myoma size, had a greater risk compared with EUA performed in patients with almost 2 times greater myoma size. In addition, there is a risk of tubal peritoneal infertility on the background of adhe-
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References