

Amenorrhea incidence among symptomatic premenopausal women with uterine fibroids after uterine artery embolization (UAE). Our experience

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Summary

Objective: To study the impact of uterine artery embolism (UAE) for fibroids on menstrual cycle and cases of amenorrhoea in premenopausal women. **Materials and Methods:** One hundred forty-five premenopausal women, aged between 38-50 years, who underwent UAE were recruited in this study. Hormonal status was evaluated by means of AMH and FSH pre-procedural, three months, six, and 12 months after UAE. Menstruation abnormalities and life quality post-procedure were noted and evaluated based on a questionnaire. **Results:** AMH as well as FSH values 12 months post-procedure were the same compared to the pre-procedure levels. The authors found no case of permanent amenorrhea. **Conclusion:** Although the study results may be able to confirm the preservation of ovarian reserve and normal menstruation after UAE in premenopausal women, it should be considered as a possible menstruation treatment option of symptomatic fibroids.

Key words: Uterine artery embolization; Uterine fibroids

Introduction

The transition from reproductive age to menopause is a continuous process often accompanied by menstrual cycle disorders. Menstrual cycle disorders are one of the most common problems of women of reproductive age, with a frequency of approximately 5% of the female population [1]. These are displayed mainly with the forms of excessive blood loss during menstruation, prolonged menstruation, and blood loss between periods. By the term menorrhagia we define excessive blood loss, in more than 80 ml during menstruation. It is a chronic problem, usually inadequately treated, consisting up to 20% of all medical gynecological visits to health services and thus has a direct impact on the healthcare economy [2, 3]. Atypical hemorrhages occurring during the perimenopausal period of a woman's life are subject to diagnostic research that varies in terms of its invasiveness and is based greatly on clinical examination, ultrasound, on hydrosoundography, and MRI [4, 5]. Among anatomical lesions that can cause abnormal uterine bleeding (AUB), falling fibroids, endometrial polyps, endometrial hyperplasia, endometrial cancer, adenomyosis, and the atrophic endometrium are included [4, 5]. Uterine fibroids are of the most frequent female genital tract symptomatic disorders usually presenting by means of heavy menstrual bleeding, abdominal pain, anaemia, pressure

symptoms, and negative effect on woman's quality of life [6, 7]. Their prevalence varies from 40 to 60% in women of reproductive age [8]. Pharmaceutical methods and imaging directed destruction methods of fibroids by high frequency ultrasound, laser, cryopoeisis, or thermal disaster are under investigation and are constantly evolving [9].

The choice of treatment depends on many medical and non-medical factors such as age, wish for childbirth, severity of symptoms, size, number and position of fibroids, as well as is associated with medical problems, probability of malignancy, and desire to maintain the uterus [9]. Uterine artery embolization (UAE) to treat bleeding caused by gynaecological or obstetric reasons, is referred as a minimally invasive treatment alternative to surgery and has been applied since 1979 [10-12]. The goal of this study was to investigate the association of UAE and occurrence of abnormal menstruation in premenopausal women until amenorrhea in the post-procedure time.

Materials and Methods

Perimenopausal women with symptomatic fibroids without desire for future pregnant after having been tested by imaging and endometrial biopsy in order to rule out the malignancy were selected for UAE. Larger fibroids (>15 cm) are expected to shrink, but their final size could also cause pressure symptoms, so they were considered as a relative contraindication. One hundred forty-

five premenopausal women between April 2008 until December 2017, with the following presenting symptoms hemorrhage anemia (60%), pain (26.67%), dysmenorrhea, dyspareunia, uterine sensitivity or a combination of the above (13.33%) were recruited in this study. Clinical diagnosis of fibroids was based on bimanual pelvic examination followed by an imaging test to confirm the diagnosis, as vaginal ultrasound and MRI. All participants had signed a written consent form before the UAE and were offered an MRI preoperatively. Measurements of AMH and FSH were made on the third day of their menstrual cycle before UAE. The mentioned hormonal status (AMH, FSH) was evaluated after UAE in time intervals of one, three, six, and 12 months. All women which participated in the study underwent MRI at one, three, six, and 12 months after UAE, where myoma volume and deterioration characteristics of the myomas were examined and evaluated. The occurrence of normal menstruation or menopausal symptoms and the life quality was recorded based on a questionnaire one, three, six, and 12 months postoperatively.

The UAE is held in Radiology Department by experienced interventional radiologist (VDS), lasts about 50-75 minutes, and includes bilateral uterine artery catheterization through a single percutaneous puncture of the right common femoral artery after local anaesthesia, using catheters of 4F diameter, with specific care concerning the patient's protection (flat-panel angiography unit, short-time radiation, avoidance of angiography runs). In the radiology department it has been estimated that ovarian irradiation entrance dose is about 100-700 mGy and exit dose about 7-35 mGy, comparable to other diagnostic tests. After the procedure, the woman remains in bed for six hours until haemostasis is confirmed at the catheter entry site and is given analgesics. In 30% the pain can be serious and requires drug analgesics. The patient can leave the hospital the same or next day with instructions because to the end of the first week, fever, shivering, increased secretion, and pain may occur. The post-embolization syndrome includes severe pain, fever, and leucocytosis and occurs in about 34% of cases. Recovery lasts for a few days, and within 2-4 days the patient returns to her daily life. Further monitoring is performed for one, six, and 12 months for the clinical evaluation of symptoms and imaging control of the fibroids size. The purpose of the first visit is the early diagnosis of pelvic inflammation.

Results are expressed as clinical (improvement of bleeding and pressure symptoms) and as imaging (decrease in uterine and fibroids size). Sometimes even a small decrease in fibroid size can cause significant difference in symptoms. Technically embolization is achieved at 95-100%. The main technical problems are the difficulties in catheterization and the spasm of the uterine artery.

The reduction of fibroid size depends on the degree of degeneration. Fibroids with adequate vascularisation, as seen in MRI, are expected to shrink more than those with degeneration. Generally after UAE, the fibroids shrink by 40-70% and the uterus size by 40-60%. Over time, shrinkage continues to increase. Relief of symptoms is expected to be approximately in 90%. In particular, menorrhagia stops in 91-100% (132) of cases, while symptoms as flatulence, pelvic pressure, and urinary frequency are reduced to 92-100% (133).

Results

The results are expressed as clinical (improvement of bleeding and pressure symptoms) and as imaging (decrease in uterine size and fibroids). Sometimes even the small de-

crease in fibroids size can cause significant difference in symptoms. Technical intervention is achieved at 100%. The main technical problems are the difficulties in catheterization and spasms of the uterine artery. The reduction in fibroid size depends on the degree of degeneration. Fibroids with good vasculature, as seen in MRI, are expected to shrink more than those with degeneration.

According to the present findings after UAE, the fibroids shrank by 60-70% and the size of the uterus from 50-60%. Over time, shrinkage continues to increase. Remission of symptoms is expected to be close to 98%. In particular, menorrhagia improved in 95-100% of the cases, while the symptoms (flatulence, pelvic pressure, and frequency) are reduced to 91-100% depending on how the outcome is calculated. The size of the uterus does not appear to be a determining factor, because remission of the symptoms is also common in patients with a matrix uteri greater than 24 pregnancy weeks. These results are also confirmed by studies of the past two years, which indicate that patients are satisfied at 98-1000%. UAE also has a beneficial effect in cases of adenomyosis, although there is not much experience. In series of 28 patients with genuine adenomyosis reported an improvement in 95.3%. It should be noted that there are no long-term data, although follow-up work up to 48 months shows high rates of satisfaction for women. The reappearance of fibroids reaches 4%, but is believed to be due to the increase in the size of old incomplete embolized myomas and adenomyosis. The main failure factor was not the initial size of the fibroids but the failure shrinking them below 30% of the original size. In three cases it was obligatory to repeat the UAE procedure due to anatomical myoma position intraligamentary.

According to the present laboratory, hormonal measurements were founded at increasing levels, of FSH until to third month and approaching the initial before UAE level 12 months post-procedure. AMH values were minimally decreasing between one and three months and reached the initial level three months post-intervention. Concerning the occurrence of amenorrhea no case was noticed in women < 45 years, but only 0.6% reported transient amenorrhea in women older than 45 years and only in the time interval from three months

Discussion

UAE constitutes a minimally invasive treatment for the uterine fibroid tumors. [13, 14] For the first time in 1989, French Ravina began to apply the preoperative method in myochemistry to reduce intraoperative hemorrhage and noted that in many cases there was a shrinkage of fibrin and the need for surgery was removed. In 1997 Goodwin published the first systematic UAE study. Since 2002, there are about 400 works on UAE in the treatment of fibroids in 10,000 patients [15]. By April 2005, it was estimated that more than 50,000 embolisms were performed in 17 differ-

ent countries. The goal of UAE is to reduce pain and pressure symptoms, as well as to reduce bleeding [16].

Fibroid tumors, which are also known as myomas, are benign tumors that arise from the muscular wall of the uterus. It is extremely rare for them to become cancerous. More commonly, they appear with heavy menstrual bleeding, pelvic pain, and pressure on the bladder or bowel. In a UAE procedure, the small particles of embolization agent are injected through a thin and flexible tube which is called a catheter. This catheter blocks the arteries that provide blood flow, causing the fibroids to shrink. Almost 96% of women with fibroids experience relief of their symptoms [17]. Because of the effect that uterine fibroid embolization cause in fertility, it is not fully understood, hence UAE is typically offered to women who are not no longer interested in becoming pregnant and want or need to avoid having a hysterectomy. There is still a large number of specialists who claim that this procedure is applicable for women who wish to become pregnant, as will be explained below, in their opinion, fibroid embolization does not alter fertility [18].

The frequency of complications is very low. There are several retrospective and prospective studies, as well as case reports referred to complications. In general, the complications involve either catheterization or the effects of uterine ischemia that can cause fibrotic necrosis and the appearance of septic imaging. Finally, other organs, especially the ovaries, may be influenced. The reported deaths after embolization are extremely rare (1:1600) and are mainly related to pulmonary embolism, which may be due to the effect of necrotic tissue on activation of the coagulation mechanism and on infection [19, 20]. The complications of catheterization are rare (< 1%), such as hematoma, allergy to contrast media, and pseudoaneurysm or vessel separation [19, 20].

Uterine fibroids abortion occur in 5% of cases and can cause inflammation requiring curettage or hysterectomy. [21, 22]. The necrotic tissue, if not removed on time, may become infected and the condition becomes severe. Cases with submucosal fibroids should be treated hysteroscopically. Ischemia can cause endometritis, pelvic inflammation, and pyometra with poor outcome, otherwise hysterectomy is prescribed [21, 22].

No predictive factors have been identified to predict this complication, but it seems to be necessary before embolization to check and treat infections of the lower genital and urinary tract and to avoid the procedure in the presence of inflammatory mass.

A chronic excretion due to fibroid fistula and communication with the endometrial cavity has been reported, which was treated hysteroscopically. Finally, ovarian failure can occur from the embolization of the ovarian-vasculating branches. It has been reported that in 11% there is extra circulation between the ovaries and the uterus, while in 5% the ovaries are vascularised exclusively by branches of the

uterus [23, 24].

Transient or permanent amenorrhea refers to rates that vary according to the age of the woman. While in young women the rates range from 0-5%, in women over 45 years they reach 43% [25-28]. It has been calculated that if a woman has a 3-11-month amenorrhea, then menopause will occur (approximately 95%) within the next four years [29-36]. On the other hand, women who have an amenorrhea for one year have a 10.5% chance of having an automatic menstruation in the future if their age is between 45-49 years and 4.5% if they are over 53 years [29-40]. The transition to menopause is a period of significant changes both at the ovarian level and in the hypothalamus - pituitary - ovary axis [41]. According to the present findings the authors confirmed hormonal changes only in the early post-interventional period, no difference between AMH, as well as FSH values 12 months post-procedure compared to the pre-procedure levels and noticed no case of permanent amenorrhea.

The rates of complications following UAE are much lower than after hysterectomy, as reported in earlier studies [42-44]. In retrospective studies comparing myomectomy with UAE, the need for transfusion reached 12% and the complications ranged from 19-25% after fibromectomy versus 0 and 4.2% after UAE [42-44]. Prospective studies comparing hysterectomy and UAE in small rows showed morbidity of 34% of hysterectomy versus 14.7% of UAE and severe complications at 12% versus 4% [42-45].

In another study, serious complications occurred in 21% after hysterectomy versus 2.6% following UAE [42-45]. In both studies the recession of menorrhagia and symptoms ranged from 61-86% [43-46]. Hospitalization and the time until the return of patients to work last for about one and ten days after UAE and are significantly lower compared to surgical methods [37-40].

The co-operation between the radiologists performing embolization and the gynaecologists who investigate the patient is of great importance. Because the method is quite new and involves another specialty, many gynaecologists do not recommend it as an alternative because its ultimate effects have not yet been investigated, but women are requesting for it. However, it is significant that the reported women's loss of blood is clearly a subjective amount. Thus, studies have shown that only 35-60% of women who come with causative menorrhagia are actually and objectively suffering from this, while on the other hand a number of women suffering from menorrhagia consider it "normal" to have this increased blood loss and they are not seeking for help [42-46]. Thus it is necessary to find an objective way of measuring blood loss during menstruation, in order to eliminate the subjectivity of the patient and, on the other hand, the effectiveness of the therapeutic approaches to be quantifiable.

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