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The Comparison of Ovarian Reserve After Uterine Artery Embolization and Hysterectomy for Uterine Fibroma

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Abstract

Background: The purpose of this study was to compare the ovarian reserve before and after uterine artery embolization and hysterectomy for uterine fibroma treatment.

Methods: After obtaining the approval of the Ethics Committee of Kermanshah Medical University, this study was carried out in Imam Reza Hospital. Between March 2011 and May 2013, 66 women who suffered from symptomatic fibroma were studied. Hysterectomy with retained ovaries was done on 33 patients and uterine artery embolization (UAE) was done on the other 33 patients. The levels of hemoglobin (Hb), follicle stimulating hormone (FSH) and ovarian follicle size before and 6 months after the operation was measured. Vaginal bleeding, reintervention, hot flash and cost in both procedures were studied.

Results: No significant difference was observed after 6 months between the two groups (P = 0.356). In each group one case with FSH above 10 IU/L was observed. The existence of dominant follicle and the size of it was the same in the two groups (P = 0.390). But the level of Hb was higher in women under embolization 6 months after intervention (P = 0.001). The average level of pain after hysterectomy was higher than embolization. The cost of embolization was 12 times higher than hysterectomy.

Conclusion: This study indicated that UAE in young women had no impact on the ovarian reserve and did not increase the level of FSH. Long term studies regarding reproductive assessment and menopausal age in women with history of UEA are necessary.

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Introduction

Uterine fibroma is a benign tumor that has a relatively high prevalence, so that it occurs almost in 50% of women of different races (especially black women). In the U.S., 30-40% of hysterectomies that performed annually (200,000) are due to fibroma [1]. The most common complication after uterine fibroma is menstrual disorders especially menorrhagia that can lead to anemia [2]. Hysterectomy has so far been considered the standard method for fibroma treatment. Medical treatments such as progesterone, gonadotropin-releasing hormone agonists have also been used, but after discontinuation, the symptoms return [3]. Complications of anesthesia, surgery, prolonged hospitalization, mental problems due to absence of the uterus and fertility are some reasons that lead to search for alternative treatments for hysterectomy in the past decade. Uterine artery embolization (UAE) is one of these methods, where uterine arteries are blocked on both sides by embolic materials such as polyvinyl alcohol (PVA) or other materials. Following the blockage, blood flow is reduced, and ischemia and necrosis will occur in fibroma which has larger diameter vessels [4]. Several studies have reported effectiveness of UAE in reducing menorrhagia and pelvic pain caused by fibroma [5-9]. UAE reduces fibroma size and its complications [10, 11]. UAE has been used to control severe bleeding after childbirth (abnormal placental adhesion) or treat cervical and interstitial pregnancies as well as cesarean scar pregnancy and has had successful results [12-16]. Patients treated with UAE have shorter hospital stay and faster recovery time than patients who have hysterectomy, but there is the probability of re-hospitalization and additional treatment to control bleeding [17, 18]. One concern after UAE is its effect on ovarian function. Previous studies have had conflicting results. A number of studies on ovarian function after UAE have reported no particular changes [19, 20]. It is said that adding ovarian artery embolization to uterine artery embolization will not accelerate the onset of

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Table 1. Patient Characteristics at Baseline

	Hysterectomy (n = 33) Mean	Embolization (n = 33) Mean	P value
Age (y)	36.21 ± 1.516	35.45 ± 4.009	0.485
Parity (n)	3.32 ± 0.822	3.10 ± 1.103	0.382
Hb (mg/dL)	10.64 ± 1.212	10.32 ± 1.586	0.359
FSH(IU/L)	4.42 ± 2.293	4.12 ± 2.861	0.641
Follicle size (mm)	18.48 ± 0.870	18.97 ± 1.425	0.395

menopause [21] and it has no effect on follicle stimulating hormone (FSH) level and ovarian reserve in young women [19, 22], while other studies suggest that there is the possibility of decreased ovarian activity, incidence of menopause symptoms, amenorrhea and abortion, and recommend that UAE not be performed for women who intend to become pregnant [23-26]. The aim of this study is to compare FSH levels (index of ovarian function) before and after embolization and hysterectomy while ovaries are preserved.

Methods and Materials

After obtaining the approval of the Ethics Committee of Kermanshah University of Medical Sciences, the study was conducted in Imam Reza Hospital, Kermanshah. Patients with uterine fibroma and its complications were enrolled. Inclusion criteria were: age 25 - 45 years, complaining of debilitating symptoms related to fibroma such as severe bleeding, 16-week size uterus, anemia, fibroma causing pressure on pelvic organs that made the patients become candidate for abdominal hysterectomy. Exclusion criteria were: probability of pelvic malignancies, ovarian pathologies, pelvic infections, those who wanted to preserve their fertility, allergic reactions to contrast material and renal disorders. First, all patients' complete medical history were taken and gynecologic examination as well as general examination were performed. Other measures including transvaginal ultrasound, pap smear and endometrial sample examination performed for each patient to rule out malignant lesions. Preoperative ultrasound was requested to detect the number of follicles and their quality as well as fibroma size. The patients were briefed about hysterectomy and UAE methods: the high cost of embolization procedure, conditions and complications of hysterectomy, the possibility of severe bleeding, relaparotomy, severe pain and anesthesia complications (general in hysterectomy and epidural in embolization). After briefing and informing them of the cost and complications of each method, the patient was assigned to one of the groups according to her choice. In addition, demographic information of participants, the number of bleeding days, pain and pelvic pressure were recorded in data sheets. On the third day of the menstrual cycle in month before operation, FSH test was performed. Patients' Hb and Hct were recorded the night before surgery. After surgery, Apotel was injected every 8 h for the first 24 h in both groups. The amount of pain on the third day (from one to ten), early complications, days of hospitalization were also recorded. All patients were advised

Table 2. Post Procedural Outcomes (6 Months After Procedure)

	Hysterectomy (n = 33) Mean	Embolization (n = 33) Mean	P value
Hb (mg/dL)	11.22 ± 1.0509	13.72 ± 1.000	0.001
FSH (IU/L)	4.690 ± 2.403	4.321 ± 1.586	0.356
Follicle size (mm)	17.15 ± 0.364	17.22 ± 1.074	0.390

Table 3. Procedure Complications

	Hysterectomy (n = 33) Mean	Embolization (n = 33) Mean	P value
Pain after intervention (day)	6.21 ± 1.111	4.00 ± 1.00	0.001
Hospital stay duration (day)	3.090 ± 2.359	1 ± 0.523	0.001
Cost ($) Insurance	120	1,460	0.001
Return to work (day) after intervention	27.181 ± 4.738	8.06 ± 2.481	0.001
Reintervention	1	2 (6.06%)	0.492
Flashing	5 (15.15%)	2 (6.06%)	0.007
Bleeding days	0	32 (94%)	0.001
Bleeding reduction	33 (100%)	32 (94%)	0.721
Pelvic pressure reduction	31 (93.93%)	28 (85%)	0.830

to return to the clinic of Imam Reza Hospital for visit every 2 weeks. If complications including severe pain, hematoma, fever, infection, urinary problem and bleeding occur, they can be recorded and treated by researcher. A telephone number was given to each participant to contact if they had a complaint or a special problem. Iron supplement (two tablets a day) was prescribed for them at the time of discharge. Six months later, the patients were called to return to the clinic for a free examination and tests. The patients' FSH levels and Hb level were checked. Ultrasound was performed again to detect follicle size and quality. For symptoms such as hot flashes, pressure, pain, bleeding, additional measures such as hormone therapy, re-operation, rehospitalization, time to return to work, symptoms of hot flashes and the total cost that patients endured for the whole treatment were studied. FSH levels were studied in two groups. According to mean and standard deviation of two groups based on Healey study, with 95% confidence and 90% power, $(1.96 + 1.28)^2$ $(1^2 + 1.8^2)/2.1^2 = 3.24^2$ $(4.24)/(9.9 - 7.8)^2 = 11$, at least 11 patients were needed in each group and totally they were 22 patients. Given that age was considered as a confounding variable, 33 patients in each group and 66 patients were totally studied [27].

Results

This study was conducted in 2011-2013 in Imam Reza Hospital, Kermanshah after obtaining the approval of the research council and Ethics Committee of University of Medical Sciences. Thirty-three patients were assigned to hysterectomy group with ovarian preservation, and 33 patients were assigned to arterial embolization group. The mean age and parity in embolization group were less than those in hysterectomy group (Table 1). Patients with lower age and fewer children tended to choose embolization. Before intervention, Hb mean in both groups was around 10 mg/dL and FSH level on the third day of the menstrual cycle was also similar in both groups and was around 4 - 5 IU/L. Low FSH level in patients was due to the fact that their mean age was low. None of them were in perimenopausal period (age < 45). Mid-cycle ultrasound in a month before intervention in both groups indicated dominant follicle in mid-cycle and follicle size was similar in both groups (P = 0.395) (Table 1). Length of hospital stay was about 3 days in patients who underwent hysterectomy and 1 day in embolized patients (P = 0.001). It took on average 17 days for patients who underwent hysterectomy to return to work (Table 2). However, patients who underwent embolization improved faster due to no surgical and anesthetic problems (8 days) (Table 2). Six months after intervention (hysterectomy and embolization), participants were assessed again in terms of FSH level, follicle size and Hb level. After 6 months, no significant difference was seen in FSH level between two groups (P = 0.356). In each group, there was a case with FSH over 10 IU/L. Although dominant follicle and its size were similar in both groups (P = 0.390), Hb level was higher in women who underwent embolization 6 months after intervention (P = 0.001) (Table 3).

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Two women who had undergone embolization were treated by hormone therapy, one case for spotting and one case for continued bleeding. Also one woman who underwent hysterectomy had wound infection and wound dehiscence. The average amount of pain after hysterectomy was higher than that of embolization (6.21 ± 1.111 vs. 4.00 ± 1.00). The cost of embolization was much higher than that of hysterectomy ($1,460 vs. $120) (Table 2). The cost of hysterectomy is about $120 due to the fact that it is covered by insurance, so the cost of embolization is 12 times greater than that of surgery. Hot flashes in women were more frequent in women who underwent hysterectomy (5 (15.15%) vs. 2 (6.06%)). Six months after intervention, women who underwent embolization, on average, had a 6-day period; only in one case embolization did not reduce bleeding.

Discussion

UAE has been used as a minimally invasive therapy for uterine fibromas over the past decade. Studies have recommended this method due to its fewer complications, reduced hospitalization time and faster recovery [28]. But the impact of this technique on ovarian function is not much known. The aim of this study was to compare the effect of UAE and hysterectomy with ovarian preservation. Before intervention, no significant difference was observed between two groups in FSH levels (P = 0.641). Patient follow-up 6 months after hysterectomy and embolization revealed that although FSH levels were slightly higher in patients who underwent hysterectomy, there was no significant difference in FSH levels between patients who underwent hysterectomy and patients who underwent embolization (P = 0.356). Also this study showed that in 33 patients who had undergone embolization, FSH levels were similar before and after intervention. This finding shows embolization had no significant effect on ovarian function (P = 0.613). According to Hehenkamp et al in premenopausal women with a mean age of 45 years, both hysterectomy and embolization decrease ovarian reserve equally [24]. Spies believed age over 45 years during embolization is the reason for decreased ovarian reserve [29]. Rashid et al did not find any evidence for decreased ovarian reserve a year after embolization [30]. In a recent study, there was no significant difference in FSH levels between two groups before (P = 0.641) and after (P = 0.356) intervention. No increase in FSH was due to the fact that patients were under 40 years old. According to Tulandi and Messina et al, there is a possibility that menopause would begin after embolization [31, 32]. Goodwin has mentioned that the likelihood of risk for permanent ovarian failure after embolization is less than 2% [33]. In two studies, women underwent UAE and myomectomy for uterine fibroma and were compared after intervention in terms of reproductive status. They compared women who underwent UAE with myomectomy. In myomectomy, more pregnancy and childbirth rates and fewer abortions and lower FSH levels were observed, therefore they recommended that embolization be performed for women who have enough children [8, 34]. If the ovarian arteries are blocked besides uterus arteries during UAE, there is increased probability of FSH increase and menstrual disorders [35]. Mara compared UAE with laparoscopic uterine artery ligation to treat fibroma and concluded that there was no difference between two methods in terms of abortion rates and pregnancy rate and even birth weight was higher in embolization group [36]. Given that patients were young, increased FSH was not noticeable. In our study, parity was lower in women treated with embolization, which shows these women have additional tendency to preserve their uterus and fertility. Hb was similar in both groups before intervention, but 6 months after intervention, Hb levels were increased in patients who underwent embolization. There is usually bleeding during hysterectomy that leads to aggravated postoperative anemia and prolonged recovery. Days of pain were significantly less in embolized patients than in those who underwent hysterectomy. Days of pain were more in a small number of patients who had large size fibroma and underwent embolization, they needed more analgesics, but generally the amount of pain in the hysterectomy group was severe (P = 0.001).

In a recent study, the mean time to return to work in patients who underwent hysterectomy was more than those who underwent embolization. Conversely, Beinfeld showed the recovery time and return to work were more in patients who underwent embolization. It seems that this difference is due to differences in recovery definition. In our study, recovery is the time that takes the patients to return to their daily activities, which was higher in hysterectomy group. But Beinfeld defined recovery as the time when there was no bleeding or no other medications were used [37]. In our study, amount of the bleeding and pelvis pressure significantly reduced in both methods after six months; only there was a case of failure in embolization group due to continuous heavy bleeding. In our study mean cost of embolization was generally more than that of hysterectomy. The cost of embolization, not covered by insurance, is about 12 times greater than the cost of hysterectomy. But Beinfeld considered embolization cost-effective for uterine fibroma due to its lower costs [37]. There was only a case of wound infection and incision opening that caused rehospitalization and led to increased costs and prolonged time of return to work. No case of uterine rupture or emergency hysterectomy was seen in six-month follow-up of patients.

Conclusion

This study showed that UAE in young women does not affect ovarian reserve and does not increase FSH levels. However, long-term studies are needed to investigate reproduction and

menopausal age in women who have UAE history.

Disclosure

This study disclosed any potential conflicts of interest and commercial affiliation.

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