

Comparison of efficacy of different embolic agents on uterine leiomyoma

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Summary

The aim of this study was to explore the efficacies, postoperative side effects, and complications of uterine artery embolization (UAE) treatments for uterine leiomyoma (UL) with different embolic agents. The study included 107 patients with UL that were treated with UAE with polyvinyl alcohol (PVA group) or pingyangmycin lipiodol emulsion and silk-segment (PLES group). Six months later, the improvement rate of anaemia, the menstrual improvement rate, the incidence rate of fever, the disappearance rates of compression symptoms and abdominal symptoms in the PVA group were 93.8%, 94.7%, 22.0%, 60.0%, and 88.9%, respectively, which showed no significant difference from those in the PLES group (90.5%, 92.3%, 84.8%, 53.3%, and 81.3%, respectively). The incidence rate of fever after embolization in PVA group was significantly lower than that in PLES group ($\chi^2=41.958$, $p = 0.000$). However, the efficacy, improvement rate of symptoms, and postoperative side effects of two groups showed no significant difference ($p > 0.05$). PVA and PLES have significant efficacy for UAE treatment on patients with UL.

Key words: Hysteromyoma; Embolization; Polyvinyl alcohol; Pingyangmycin lipiodol emulsion.

Introduction

Uterine leiomyoma (UL) is the most common benign tumor occurs in female reproductive system. It easily occurs in women of childbearing age with an incidence rate of 20% to 30% in women that are more than 35 years of age and a much higher incidence rate of 51.2% to 60% in women that are 40 to 50 years of age. There are three ways for treating UL, including drug treatment, interventional therapy, and surgical treatment. Drug treatment cannot eliminate or radically cure the tumor generally and often result in recurrence or growth as the sex hormone levels recover after drug withdrawal. Surgical therapy, including hysterectomy, partial hysterectomy, myomectomy, and hysteroscopic surgery, are effective but will seriously affect the patient's quality of life if the treatment is improper. Uterine artery embolization (UAE) is rapidly developed new technology in minimally invasive treatment in the recent ten years [1]. It can maintain the uterus and can be carried out under local anesthesia, with no risk of excessive loss of blood or demand of blood transfusion, and the patients can rehabilitate quickly [1-4]. At present, UAE is a relatively safe and effective method in treatment of UL. In 1995, Ravina *et al.* [5] have firstly reported the application of polyvinyl alcohol (PVA) in embolization of UL. As reported by Society of Cardiovascular and Interventional Radiology (SCVIR) [6], there are 800 patients with UL worldwide receiving UAE therapy in 1998. The short-term

total effective rate is 90%, and the mean reduction of myoma size is 50%. With the development of interventional treatment, the efficacy of UAE in treating UL has been accepted by the majority of gynecologists and patients [7, 8]. At present, there are many kinds of embolic agents for treating UL, with different action principles. There is no unified standard for choosing which kind of embolic agent. The efficacy, postoperative side effects and complications of different embolic agent are rarely reported.

In this study, clinically common embolic agent PVA and pingyangmycin lipiodol emulsion and silk-segment (PLES) were used for UAE of UL. The efficacy, postoperative side effects, and complications of two embolic agents were compared. The objective is to provide an experimental basis for clinical application of these embolic agents.

Materials and Methods

General information

The study enrolled 107 patients with UL from January 2009 to June 2011, aged from 27 to 50 years. This study was conducted in accordance with the declaration of Helsinki and with approval from the Ethics Committee of Baotou Medical College. Written informed consent was obtained from all participants. There were 52 cases of multiple myoma and 55 cases of single myoma, with a tumor size of $2.1 \times 2.2 \times 2.0$ cm to $12.0 \times 11 \times 13$ cm. There were 95 patients accompanied with various symptoms, in which 45 patients had profuse menstruation or menstrual extension, 25 patients had frequent micturition, urgent micturition or constipation

Revised manuscript accepted for publication December 15, 2014

Table 1. — General data of the subjects ($\bar{x} \pm s$).

Groups	Age (years)	Myoma size (cm ³) *	Location of myoma			Number of myomas	
			Submucous myoma	Subserous myoma	Intramural myoma	Multiple	Single
PVA (n=41)	41.4±4.8	91604.8±59372.3	2	5	34	21	20
PLES (n=66)	40.3±5.7	75677.3±68748.4	7	8	51	31	35
t / χ^2	$t=1.029$	$t=1.226$		$\chi^2=1.168$		$\chi^2=0.183$	
p	0.306	0.223		0.558		0.669	

Groups	Profuse menstruation or menstrual extension	Symptoms Hypogastralgia	Compression symptoms	Hemoglobin concentration (g/L)	
				90~120	60~90
PVA (n=41)	19	10	9	15	1
PLES (n=66)	26	15	16	18	3
t / χ^2		$\chi^2=0.259$		$\chi^2=0.581$	
p		0.878		0.446	

PVA: polyvinyl alcohol; PLES: pingyangmycin lipiodol emulsion and silk-segment.

*Sum of diameters of multiple myomas, which was converted into diameters of single myoma [11];

hysteromyoma volume was calculated with the formula of $4\pi abc/3\text{cm}^3$ where a, b, c represent the three-dimensional diameters of myomas [12].

and other compression symptoms, and 25 cases with hypogastralgia. Among the 45 cases with profuse menstruation or menstrual extension, 37 cases were anaemic with hemoglobin in 90~129 g/L (n=33) or 60~90 g/L (n=4). In terms of the location of the myoma, 107 cases of UL could also be classified into submucous myoma (n=9), subserous myoma (n=13), and intramural myoma (n=85). Eight patients had received a myomectomy in the last two to 14 years. The general information of patients in the two groups are listed in Table 1. There was no statistical difference of the general information between the two groups ($p > 0.05$).

Inclusion criteria

1) Patients with UL have symptoms such as profuse menstruation, menstrual extension, anemia, frequent micturition, urgent micturition, hypogastralgia, and other symptoms. 2) Patients with UL revealing asymptomatic but requesting for therapy. 3) Patients with UL before menopause, married, and without contraindications for artery embolization. 4) Patients with UL voluntarily agreed to undergo UAE treatment.

Surgical methods

Uterine artery embolization was carried out about one week after the end of menstruation of each patient. In PVA group, 100-300 mg of 355-550 μm PVA was used [9]. In PLES group, PLES was used. According to leiomyoma size and richness of blood supply, the dosage of lipiodol was determined as 8-20 ml (average 12 ml). The dosage of pingyangmycin was 8-16 mg (average 14 mg). A 7-0 silk was cut into one-mm segment for use. Using Seldinger technique, 4-F multipurpose catheter and super-smooth guidewire were intubated through unilateral femoral artery and punctured the contralateral uterine artery for ultraselection of intubation. Circuitous uterine artery or disorderly blood vessel shadows could be observed in the tumor by angiography. Embolic agents was injected into uterine artery under fluoroscopy until the blood flow slowed down and disappeared. Then guidewire-looping technique was used for contralateral UAE, and the same embolization was carried out under angiography. Finally, pelvic arteriography was performed again. Nonvisualization of bilateral uterine artery indicated complete embolization.

At one, three, and six months after the embolization, each patient underwent B-ultrasound and gynecological examinations and the anaemic patients had their hemoglobin reassessed at for to six days after menstruation.

Evaluation of therapeutic efficiency

Evaluation of therapeutic efficiency [10] was mainly based on the clinical symptoms and the variation of the myoma size. At six months after embolization, the reduction of myoma volume was more than 50% and menstrual cycle and flow recovery could be considered as marked effectiveness; the reduction of myoma volume was 20%-50% and the menstrual cycle and flow that were close to the normal level could be considered as effective, and the myoma volume reduction less than 20% and the menstrual cycle and flow that did not change significantly were considered as invalid.

Results

Clinical efficacy

Improvement of symptoms: Patients were followed up for one to 30 months with a mean of six months and there were 88 cases followed up for more than six months. Before embolization, the mean hemoglobin concentration in patients with mild to moderate anemia (n=37) was 101.2 g/L in the PVA group and 99.8 g/L in the PLES group. However, at three months after embolization, the mean hemoglobin concentrations were restored to 123.5 g/L and 121 g/L, respectively. The anaemic improvement rates were 93.8% (15/16) and 90.5% (19/21) in the PVA and PLES groups, respectively, showing no statistical difference between each other ($c^2=0.000$, $p=1.000$) (Table 2).

Reduction of myoma size: Before and after embolization, the three-dimensional diameters of UL were measured using B-ultrasound imaging and then were compared between the two groups. The response rate of PVA was 97.5% (40/41) in the PVA group, showing no statistical difference from that of PLES 97.0% (64/66); $c^2=0.000$, $p=1.000$) (Table 3).

Postoperative side effects

Embolism syndrome presents nausea, vomiting, fever and abdominal pain after embolization. Twenty-one patients in the PVA group presented the embolism syndrome,

Table 2. — *The improving rates of the two groups after embolization.*

Groups	Time points	Profuse menstruation or menstrual extension	Hemoglobin concentration (g/L)		Frequent micturition and urgent micturition (n=25)	Hypogastralgia (n=25)
			90–120 (n=33)	60–90 (n=4)		
PVA (n=41)	Before embolization (cases)	19	15	1	10	9
	1 month after embolization (cases)	14	10	1	9	8
	3 months after embolization (cases)	4	4	0	7	3
	6 months after embolization (cases)	1	1	0	4	1
	Improvement rate at 6 months after embolization	94.7% (18/19)	93.8% (15/16)		60.0% (6/10)	88.9% (8/9)
PLES (n=66)	Before embolization (cases)	26	18	3	15	16
	1 month after embolization (cases)	20	12	2	14	15
	3 months after embolization (cases)	8	6	0	10	8
	6 months after embolization (cases)	2	2	0	7	3
	Improvement rate at 6 months after embolization	92.3% (24/26)	90.5% (19/21)		53.3% (8/15)	81.3% (13/16)
	χ^2 value *	0.000	0.000		0.000	0.000
	<i>p</i> value *	1.000	1.000		1.000	1.000

* Comparison of the improvement rate of six months after embolization between PVA and PLES groups.

Table 3. — *Induction of hysteromyoma after embolization in the PVA and PLES groups.*

Groups	Time points	No marked induction of hysteromyoma (invalid)	Induction of 20%–50% (Effectiveness)	Induction of >50% (Marked effectiveness)	Myoma elimination (Marked effectiveness)
PVA (n=41)	1 month after embolization (cases)	4	33	4	0
	3 month after embolization (cases)	3	24	12	2
	6 month after embolization (cases (%))	1 (2.4%)	10 (24.4%)	28 (68.3%)	2 (4.9%)
PLES (n=66)	1 month after embolization (cases)	6	41	19	0
	3 month after embolization (cases)	4	27	29	6
	6 month after embolization (cases (%))	2 (3.0%)	16 (24.2%)	40 (60.6%)	8 (12.1%)
	χ^2 value *	0.033	0.000	0.645	0.828
	<i>p</i> value *	0.856	0.986	0.422	0.363

*Comparison of the induction of hysteromyoma at 6 month after embolization between PVA and PLES groups.

accounting for 51.2%, which was statistically significant from that of the PLES group (84.8%, $c^2=14.175$, $p=0.000$) (Table 4).

There was no patient complicated with ectopic embolization or sepsis or other serious complications postoperatively.

Follow-up

Eighty-eight cases were followed up for more than six months and the longest follow-up period was 30 months. No recurrence was observed in the embolized myomas during the follow-up period. New myomas were found at 20 and 28 months after embolization in two patients with multiple myomata, and one of them had underwent myomectomy 16 years ago.

Discussion

In this study, two kinds of clinically common embolic agents PVA and PLES are used in treatment of 41 and 66 cases of UL, respectively. The efficacy of embolic agent, postoperative side effect and complication between the two groups are compared. Results show that, UAE with

Table 4. — *Incidence rate of embolism syndrome after hysteromyoma embolization in the PVA and PLES groups.*

Groups	Postoperative fever	Nausea	Vomiting	Abdominal bearing-down pain
PVA (n=41)	9 (22.0%)	15 (36.6%)	14 (34.1%)	21 (51.2%)
PLES (n=66)	56 (84.8%)	32 (48.5%)	28 (42.4%)	46 (69.7%)
χ^2 value	41.958	1.454	0.727	3.689
<i>p</i> value	0.000	0.228	0.394	0.055

PVA and PLES have obvious efficacy in treatment of UL, with no significant difference between the two groups ($p > 0.05$), which is similar with reported results (6, 13, 14). The side effects of UAE are nausea, vomiting, and abdominal pain, and there is no significant difference between the two groups ($p > 0.05$). The incidence rate of fever in PLES group is significantly higher than in PVA group ($c^2 = 41.958$, $p = 0.000$), which is related to releasing pyrogenic substance by necrotic tissue and absorbance heat of necrotic tissue. Generally, the body temperature increases with the increase of necrotic tissue. The side effect

of PVA after embolization is similar with reported results [15-18]. Except for severe pain, the side effect of PLES is also similar with reported results [6, 14]. Abdominal pain is mainly caused by ischemia, injury, pain substance release, and local swelling stimulation after embolization. The degree of pain is associated with embolization degree and level. As the embolization degree is greater, it is closer to the capillary level, hence the pain is more obvious. More severe pain in PLES group may be related with the slower microsphere expansion velocity and embolization degree close capillary level.

There are many reports on UAE in treatment of UL. Goodwin *et al.* [7] have reported that, the symptom-improving rate of UAE on UL is 81% and the myoma shrinks off by 92% at 18 months after surgery. The present results show that, PVA and PLES have obvious short-term efficacy in treatment of UL. However, the long-term efficacy of UAE and its effect on newborn myoma should be further confirmed [12]. The main side effects of UAE are embolism syndromes (nausea, vomiting, fever, and abdominal pain), which occur within one to two days after embolization, and are associated with the uterine ischemia. They can be relieved and eliminated by symptomatic treatment. The postoperative body temperature of patients in PVA group is about 37.5°C and drops to the normal level within two days, while it is 37.8°C to 39.6°C in PLES group and drops to the normal level within five days. Six patients in the PLES group had a postoperative temperature higher than 38.8°C, which was lowered to the normal level by using one course of antibiotics.

There are also other reported complications of UAE, such as ectopic embolism, urinary retention, purulent endometritis, sepsis, abnormal vaginal bleeding and discharge of necrotic tissues, etc. [19, 20]. No ectopic embolism occurred in this study. The occurrence of urinary retention may result from severe pain in the lower abdomen after embolization, but can be relieved as the pain alleviated. Purulent endometritis may originate from preoperative intrauterine infection or the embolic time close to the menstrual period. Thus, embolization should be carried out at one to two weeks before menstruation [21]. Sepsis is resulted from the purulent endometritis that has not been timely controlled. Irregular vaginal bleeding and discharge of necrotic tissue are mainly caused by submucosal myomas. The submucosal myomas are atrophied and necrosed after embolization, and discharged in one to three months after embolization. In this study, three cases of submucosal myomas in PLES group were self-discharged, and another four cases as well as two patients in the PVA group were shed in the uterus and extracted by vaginal forceps. The present authors believe that, embolization is better for submucosal myomas, which is consistent with the literature [22, 23].

In conclusion, PVA and PLES have obvious efficacy in UAE of UL, with high safety. There is no significant dif-

ference between two materials, but the postoperative side effects in them are significantly different. After UAE using PLES, fever should be well controlled. PVA is expensive and can be chosen in practical application according to actual situation of patients.

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