

## Original Article

# The effects of the combination of Yasmin and shaofuzhuyu capsules on MBV, endometrial thickness, and disease recurrence in hysteroscopic polypectomy patients

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**Abstract:** Objective: This study was designed to analyze the effects of Yasmin combined with shaofuzhuyu capsules on menstrual blood volume (MBV), endometrial thickness, and disease recurrence in hysteroscopic polypectomy patients. Methods: 115 patients with endometrial polyps admitted to our hospital were included as the study cohort and underwent hysteroscopic polypectomies. Based on the postoperative drug administration mode, the patients were divided into two groups, including the control group (CG, n=57) for treatment with Yasmin alone, and the observation group (OG, n=58) for treatment with Yasmin and shaofuzhuyu capsules. The two groups were compared in their endometrial thickness, MBV, disease recurrence, menstrual improvement, and adverse reactions in the different postoperative stages. Results: (1) At 3 months, 6 months, and 12 months after the operations, in addition to a lower endometrial thickness as compared with the CG ( $P<0.05$ ), the OG reported menstrual improvement rates of 70.69%, 74.14% and 96.55%, respectively, higher than the corresponding values in the CG, which were 33.33%, 40.36% and 70.18% ( $P<0.05$ ). (2) Compared with the CG, the postoperative reoccurrence rates of endometrial polyps in the OG were lower at 6 months and 12 months after the operations ( $P<0.05$ ), but no statistical difference was observed between the two groups in terms of the incidences of adverse reactions, which were 8.62% in the OG and 7.02% in the CG ( $P>0.05$ ). Conclusion: After hysteroscopic polypectomy, the combination of Yasmin and shaofuzhuyu capsules, improved MBV and endometrial thickness, and disease recurrence rate was reduced with no increase in drug-related adverse reactions and a higher drug safety, which is worthy of promotion.

**Keywords:** Hysteroscopic polypectomy, Yasmin, shaofuzhuyu capsules, MBV, endometrial thickness, disease recurrence

## Introduction

A benign localized endometrial lesion with high clinical incidence [1], endometrial polyps are benign localized hyperplasia on the endometrial basal layer, and may be single or multiple. Endometrial polyps may result in irregular colporrhagia, increased menstrual volume, menostaxis, and even aciesis in females in the child-bearing age. Irregular colporrhagia is the main syndrome in postmenopausal women [2, 3].

At present, hysteroscopy has been extensively applied in the diagnosis and treatment of endometrial polyps. On this basis, the minimally invasive hysteroscopic polypectomy is devel-

oped to clearly expose the changes on the inner membranes inside the uterus, and its greater values are shown in the case of small endometrial polyps [4, 5]. Hysteroscopic polypectomy has developed into the gold standard for the clinical treatment of endometrial polyps, but requires surgeons with sophisticated endoscopic skills. Meanwhile, the recurrence rate is high after the operation can have multiple complications, which require active drug administration measures [6]. In traditional Chinese medicine, endometrial polyps are categorized within the scope of "abdominal mass", "acyesis", and treated mainly by regulating the uterine vessels, qi and blood, dispersing blood stasis and dredging collateral [7]. In this study,

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Yasmin and shaofuzhuyu capsules were combined for the treatment after hysteroscopic polypectomy in order to further reduce the postoperative recurrence rate and improve menstruation.

Previously, only the clinical efficacy of endometrial polyp treatment after hysteroscopic polypectomy was focused on, rather than the control of the postoperative recurrence rate. In this study, Yasmin was combined with shaofuzhuyu capsules to study the effects on menstrual blood volume (MBV), endometrial thickness and recurrence, which is innovative and feasible to a certain degree.

## Materials and methods

### Materials

115 patients with endometrial polyps admitted to our hospital were included as the study cohort for a retrospective analysis after they were treated with hysteroscopic polypectomies. Afterward, they were divided into the control group (CG, n=57) with an age range of 20 to 45 for treatment with Yasmin alone, and the observation group (OG, n=58) with an age range of 21 to 46 for treatment with Yasmin and shaofuzhuyu capsules according to the postoperative drug administration mode. (1) Inclusion criteria: patients diagnosed with endometrial polyps without surgical contraindications were included in this study. The diagnosis meets the diagnostic criteria for endometrial polyps [8]. The patients provided their written informed consents before participating in the study. This study was approved by the Ethics Committee of Hangzhou Fuyang Hospital of Traditional Chinese Medicine. (2) Exclusion criteria: Patients who had severe heart or liver insufficiency, patients with circulatory diseases, patients with concurrent uterine adenomyosis, uterine leiomyoma, or other organ diseases, patients treated with hormones within six months before the operation, patients who planned to get pregnant within the next two years, or patients with malignant endometrial biopsy results.

### Methods

After the hysteroscopic polypectomies, all the patients were treated with antibiotics in case of infection. The patients in the CG were orally

administered Yasmin (manufacturer: Bayer Healthcare Co., Ltd. Guangzhou Company, approval document no. GYZZ J20171071, specification: 21 tablets) at a dose of 1 pill per time for 21 d, after which, a break was required until the 5th day of menstruation. The treatment continued for 3 menstrual cycles. In addition to the treatment given to the patients in the CG, the patients in the OG were additionally orally administered with shaofuzhuyu capsules (approval document no. GYZZ Z20000085, manufacturer: Donga'ao Pharmaceuticals Co., Ltd., specification: 0.45 g\*36 capsules/box) at the dose of 3 capsules each time and 3 times a day. The drug was withdrawn during menstruation, and the treatment continued for 3 menstrual cycles.

### Observation indices

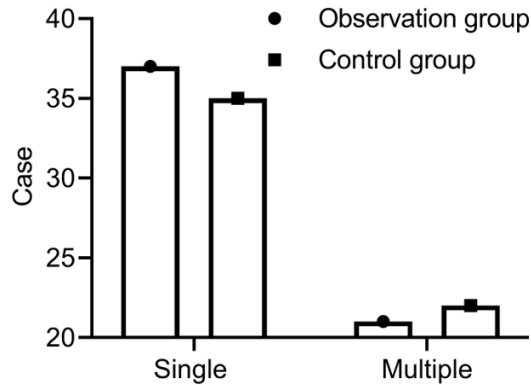
(1) Endometrial thickness: all patients were followed up for 12 months, during which, the endometrial thickness was measured before the operation and at 3, 6 and 12 months after the operation. A color Doppler ultrasound diagnostic system was used to perform vaginal ultrasonography on all the patients. The probe frequency was set to 5 MHz. The patients had their bladders moderately filled by drinking water and were in a supine position. The endometrial thickness was measured.

(2) MBV: all the patients were followed up for 12 months, during which, MBV was measured before the operations and at 3, 6 and 12 months after the operation. MBV was measured using a pictorial blood loss assessment chart in which the number of sanitary napkins used was recorded to estimate the MBV.

(3) Menstrual improvement: the two groups were compared in terms of their menstrual improvement at 3 months, 6 months, and 12 months after the operations according to following criteria: reduced or normal MBV, and regular menstruation.

(4) Recurrence: the two groups were compared for the recurrence of endometrial polyps at 3 months, 6 months, and 12 months after operation according to the following criteria: abnormal echo in the cavum uteri, a definite diagnosis as determined through pathology and a hysteroscope.

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**Figure 1.** Comparison of the proportions of single and multiple endometrial polyps in the OG and the CG. Single and multiple endometrial polyps accounted for 63.79% and 36.21% in the OG and 61.40% and 38.60% in the CG ( $P>0.05$ ).

(5) The incidence of adverse reactions: the two groups were compared in their incidence of adverse reactions during the treatment.

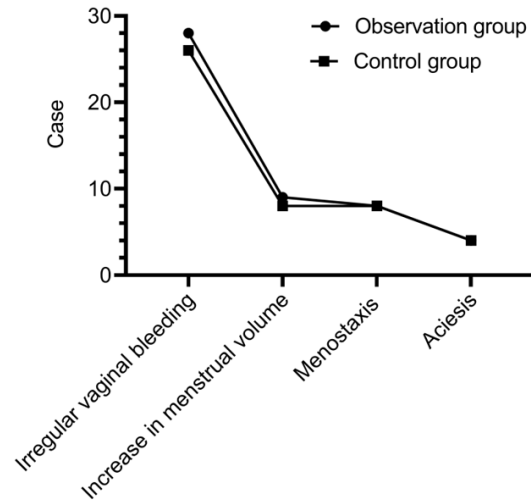
### Statistical analysis

The statistical analysis was performed with SPSS 22.0. In the case of numerical data expressed as the mean  $\pm$  standard deviation, independent-samples T tests were used for the normal distribution data, Mann-Whitney U tests were used for the non-normal distribution data, and paired tests were used for the pre-and-pro comparisons within a group; in the case of nominal data expressed as [n (%)],  $\chi^2$  tests were used for the intergroup comparisons. For all the statistical comparisons, significance was defined as  $P<0.05$ .

## Results

### Comparison of the general data in the OG and the CG

The mean ages of the patients were ( $32.58 \pm 1.32$ ) years in the OG and ( $32.56 \pm 1.29$ ) years in the CG; the polyp diameters were 0.4-5.5 cm in the OG and 0.5-5.4 cm in the CG, averaging ( $2.62 \pm 0.12$ ) cm and ( $2.59 \pm 0.13$ ) cm, respectively. The patients in the OG had an average parity of ( $1.28 \pm 0.16$ ) with a range from 1 to 3, while the corresponding values in the CG were ( $1.25 \pm 0.12$ ) and 1 to 2, respectively. In the OG, there were 37 (63.79%) and 21 (36.21%) patients with single or multiple endometrial polyps, and in the CG, the proportions were 35 (61.40%) and 22 (38.60%). The patients with



**Figure 2.** Comparison of clinical manifestations in the OG and the CG. Patients with irregular colporrhagia, increased MBV, menostaxis, and aciesis accounted for 48.28%, 15.51%, 13.79% and 6.90% in the OG and 45.61%, 14.04%, 14.04% and 7.02% in the CG ( $P>0.05$ ).

irregular colporrhagia, increases in their MBV, menostaxis, and aciesis were 28 (48.28%), 9 (15.51%), 8 (13.79%) and 4 (6.90%) in the OG and 26 (45.61%), 8 (14.04%), 8 (14.04%) and 4 (7.02%) in the CG. Between the OG and the CG, no statistical differences were observed in terms of the general patient characteristics such as average age, mean polyp diameter, average parity, onset type (**Figure 1**), or clinical manifestation (**Figure 2**) ( $P>0.05$ , **Table 1**).

### Comparison of endometrial thickness at different stages in the OG and the CG

The two groups were compared in their endometrial thicknesses before and after operations ( $P>0.05$ ); at 3 months, 6 months and 12 months after operation, the endometrial thicknesses reduced gradually and significantly ( $P<0.05$ ) in both groups, and the OG reduced significantly ( $P<0.05$ , **Table 2**).

### Comparison of the MBV at different stages in the OG and the CG

Before the operation, the MBV was ( $107.85 \pm 12.25$ ) ml in the OG and ( $107.89 \pm 12.06$ ) ml in the CG ( $P>0.05$ ); at 3 months, 6 months and 12 months after operation, the MBV gradually reduced to ( $47.05 \pm 2.56$ ) ml, ( $25.15 \pm 1.26$ ) ml and ( $20.02 \pm 1.06$ ) ml in the OG and

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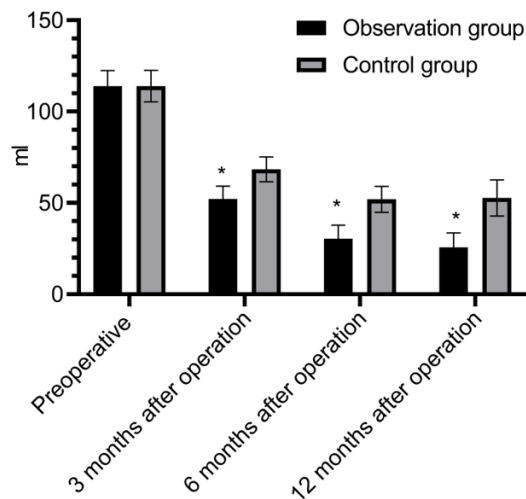
**Table 1.** Comparison of the General Data in the OG and the CG [n (%)]/( $\bar{x} \pm s$ )

Data	OG (n=58)	CG (n=57)	t/ $\chi^2$	P
Age (y)	45.26±2.28	45.96±2.16	1.690	0.094
Polyp diameter (cm)	2.62±0.12	2.59±0.13	1.286	0.201
Parity (time)	1.28±0.16	1.25±0.12	1.136	0.258
Disease type				
Single	37 (63.79)	35 (61.40)	0.070	0.791
Multiple	21 (36.21)	22 (38.60)		
Clinical manifestation				
Irregular colporrhagia	28 (48.28)	26 (45.61)	0.015	0.996
Increase in MBV	9 (15.51)	8 (14.04)		
Menostaxis	8 (13.79)	8 (14.04)		
Aciesis	4 (6.90)	4 (7.02)		

**Table 2.** Comparison of the endometrial thickness at different stages in the OG and the CG ( $\bar{x} \pm s$ , mm)

Group	Before the operation	3 months after the operation	6 months after the operation	12 months after the operation
OG (n=58)	18.19±2.09	7.15±1.02 <sup>*,*</sup>	6.25±0.58 <sup>*,*</sup>	5.12±0.18 <sup>*,*</sup>
CG (n=57)	18.12±2.12	10.25±1.25 <sup>#</sup>	9.98±0.85 <sup>#</sup>	8.86±0.68 <sup>#</sup>
t	0.178	14.583	27.530	40.472
P	0.859	0.000	0.000	0.000

Note: #indicates  $P < 0.05$  as compared with the preoperative conditions, and \*indicates  $P < 0.005$  compared with the CG.



**Figure 3.** Comparison of the MBV in the OG and the CG. The MBVs in the OG at 3 months, 6 months, and 12 months after the operation were lower compared with the CG ( $P < 0.05$ ). \* indicates  $P < 0.05$  compared with the CG.

(63.58±9.96) ml, (46.85±9.16) ml and (45.-69±9.68) ml in the CG ( $P < 0.05$ ), and the values after the reduction were far lower in the OG ( $P < 0.05$ , **Figure 3**).

### Comparison of the menstrual improvement between the OG and the CG

The menstrual improvement rate was 70.69%, 74.14% and 96.55% in the OG and 33.33%, 40.36% and 70.18% in the CG at 3 months, 6 months, and 12 months, respectively after the operations ( $P < 0.05$ , **Table 3**).

### Comparison of disease recurrence in the OG and the CG

At 3 months, 6 months and 12 months after the operations, the recurrence rates were 0%, 0%, and 1.72% in the OG and 0%, 10.53% and 21.05% in the CG; while no statistical difference was observed at 3 months after operation, the recurrence rate of endometrial polyps was lower in the OG at 6 months and 12 months after the operations ( $P < 0.05$ , **Figure 4**).

### Comparison of the incidences of adverse reactions in the OG and the CG

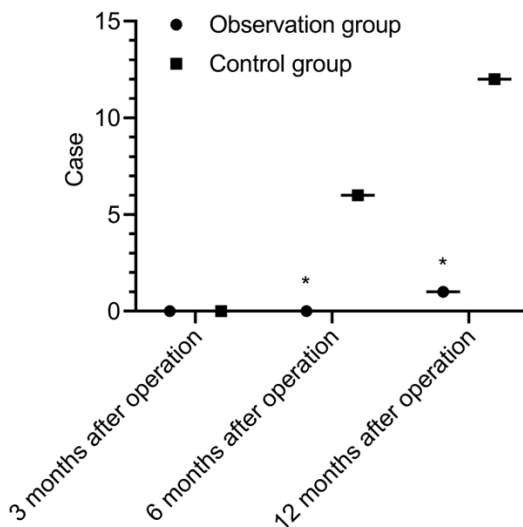
During the treatment, the OG reported 2, 2, and 1 cases of nausea, vomiting, and dizziness, for an 8.62% rate of adverse reactions. The corre-

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**Table 3.** Comparison of the menstrual improvement in the OG and the CG [n (%)]

Group	n	3 months after the operation	6 months after the operation	12 months after the operation
OG	58	41 (70.69)*	43 (74.14)*	56 (96.55)*
CG	57	19 (33.33)	23 (40.36)	40 (70.18)
$\chi^2$		16.077	13.420	14.501
<i>P</i>		0.001	0.000	0.000

Note: \*indicates  $P < 0.05$  as compared with the CG.



**Figure 4.** Comparison of the disease recurrence in the OG and the CG. In terms of the disease recurrence rate of endometrial polyps, no statistical difference was observed between the two groups at 3 months after the operations, but the reported data were 0% and 1.72% in the OG and 10.53% and 21.05% in the CG at 6 months and 12 months after the operations ( $P < 0.05$ ). \* indicates  $P < 0.05$  as compared with the CG.

**Table 4.** Comparison of the incidence of adverse reactions in the OG and the CG [n (%)]

Group	n	Nausea	Vomiting	Dizziness	Total incidence
OG	58	2 (3.45)	2 (3.45)	1 (1.72)	5 (8.62)
CG	57	2 (3.51)	1 (1.75)	1 (1.75)	4 (7.02)
$\chi^2$					0.102
<i>P</i>					0.749

sponding data were 2, 1, and 1 for a 7.02% rate in the CG ( $P > 0.05$ , **Table 4**).

### Discussion

Endometrial polyps are a type of endometrial lesion with a high incidence rate, and females over 35 years old are most commonly affected

by the disease [9]. Its clinical syndromes include postmenopausal vaginal bleeding, dripping colporrhagia, menstrual disorders, menostaxis, and an increase in the MBV. In the case of small polyps, it is possible that no clinical manifestations are seen [10, 11].

In recent years, the extensive application of hysteroscopy in the clinic has significantly improved the success rate of endometrial polyp diagnosis and treatment [12, 13]. In addition to its treatment functions, a hysteroscope also participates in the examination and direct observation of the scope of the lesions, their location, and their intrauterine morphology and appearance, and it can harvest the lesion regions for pathological examination [14, 15]. Hysteroscopic polypectomy is a commonly used operation in the treatment of endometrial polyps, and it has no impact on ovarian function, only requires a short hospital stay, has a rapid postoperative recovery, and a low incidence of complications [16]. Although hysteroscopic polypectomy has significant advantages in the treatment of endometrial polyps, there is a high recurrence rate after the procedure, so reducing the postoperative recurrence rate of this disease is still a hot issue in clinical research [17].

Yasmin is a new contraceptive mainly made of ethinylestradiol and drospirenone [18]. A 17 $\alpha$ -spironolactone derivative, drospirenone is characterized by its high affinity to the receptors of mineralocorticoid and progestational hormones compared with other drugs, and it can inhibit ovulation and achieve the purpose of contraception [19]. Secondly, drospirenone is a highly active rival of androgen receptors, which can suppress the activity of the ovaries and the production of adrenal testosterone [20]; its resistance to the activity of mineralocorticoids enables it to promote the alleviation of syndromes such as headache, breast pain, and weight gain due to its water-sodium reten-

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tion [21]. In the studies of Xin [22] et al., it was found that the oral administration of Yasmin cannot only resist various syndromes introduced by water-sodium retention, but it can also improve the symptoms of premenstrual syndrome and reduce the endometrial thickness. Nevertheless, a high recurrence rate still requires an effective method [23].

The term endometrial polyp is present in traditional Chinese medicine. According to its clinical syndromes, the disease can be categorized within the scope of “abdominal mass”, “acycy-sis”, and “uterine bleeding” with stasis in uterus vessels and uterus as the major cause. Its pathogenesis is closely associated with blood stasis, and a deficiency of the Chong and Ren Channels. Therefore, the treatment shall comply with the principle of “dispersing blood stasis and dredging collateral” to regulate the qi and blood, and dredge uterine vessels [24]. The results of this study revealed that, at 3 months, 6 months, and 12 months after the operations, the endometrial thickness and recurrence rate of endometrial polyps were lower, and the menstrual improvement rate was higher in the OG compared with the CG ( $P < 0.05$ ), indicating that the combination of Yasmin and shaofuzhuyu capsules after hysteroscopic polypectomy can improve MBV, and reduce endometrial thickness and the disease recurrence rate. Furthermore, the incidence of adverse reactions was 8.62% in the OG and 7.02% in the CG during the treatment ( $P > 0.05$ ), indicating the safety of Yasmin and shaofuzhuyu capsules as a combination treatment after hysteroscopic polypectomy. Such an insignificant difference shall be explained from the perspective of the ingredients in shaofuzhuyu capsules, including *Cinnamomum cassia*, *Ligusticum wallichii*, fennel (fried with salt), processed myrrh, rhizoma zingiberis, *Corydalis ambigua* Ch. (made with vinegar), Radix Paeoniae Rubra, excrementum pteropi (made with vinegar), cattail pollen and *Angelica sinensis*. Amongst those materials, *Ligusticum wallichii*, Radix Paeoniae Rubra, and *Angelica sinensis* are known as sovereign drugs capable of nourishing the blood for regulating menstruation, activating blood circulation and removing blood stasis; myrrh, *Corydalis ambigua* Ch., excrementum pteropi, and cattail pollen are minister drugs for removing stasis, promoting blood circulation and relieving pain; *Cinnamomum cassia*, rhizoma zingiberis, and

fennel are adjuvants to regulate qi, alleviate pain, warm the channels, and expel the cold. These medicines can jointly eliminate cold to stop pain, activate the blood circulation to dissipate blood stasis, warm the kidneys and enhance yang [25]. The addition of shaofuzhuyu capsules on the basis of Yasmin achieves a synergistic action to further improve efficacy and reduce the postoperative recurrence rate of endometrial polyps [26]. In conclusion, after hysteroscopic polypectomy, the combination of Yasmin and shaofuzhuyu capsules, improve MBV and endometrial thickness, and reduce the disease recurrence rate with no increase in drug-related adverse reactions and a higher drug safety, which is worthy of promotion.

Although this study has achieved certain results, there are also limitations. Only a small cohort was examined in this study, so the results obtained are not sufficiently representative, and further in-depth exploration is needed in the future.

### Disclosure of conflict of interest

None.

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