



Curative Effect of Mifepristone Combined with Guizhifuling Capsule in the Treatment of Uterine Fibroids

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ABSTRACT

The objective of the study was to observe the effect of mifepristone combined with Guizhifuling capsule in the treatment of uterine fibroids. Patients (160) diagnosed and treated for uterine fibroids in our hospital were enrolled as research objects. The patients were randomly divided into an experiential group and a control group, each containing 80 patients. The experiential group was treated with mifepristone and Guizhifuling capsule, and then subjected to high quality nursing. In contrast, the control group was treated with only mifepristone therapy and applied with routine nursing measures. The therapeutic and nursing effects of the two groups were compared. After the implementation of different treatment and nursing mode, the overall treatment effective rate of the research group patients was 97.50%, which was significantly higher than 75.00% of control group, $p < 0.05$. Through comparing the changes of fibroid volume before and after treatment between the two groups, the results showed that the improvement effect of the research group was significantly better than that of the control group after treatment, $p < 0.05$. The incidence of adverse reactions of the research group was significantly lower than that of control group, while the overall nursing satisfaction of the research group was significantly higher than that of the control group, $p < 0.05$. It is concluded that combination therapy of mifepristone and Guizhifuling capsule can significantly improve the treatment effect in patients with uterine fibroids.

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Authors' Contribution

YG and PG diagnosed uterine fibroids patients and classified them. YG and YS designed the treatments. YW and JH treated different groups of patients. YG and PG processed the data. YG and YS wrote the manuscript.

Key words

Mifepristone, Guizhifuling capsule, Combination therapy, Uterine fibroids, High quality nursing

INTRODUCTION

Uterine fibroids is one of the most common and frequently-occurring gynecological diseases among women aged between 30 and 50. Uterine fibroids are generally treated by surgery, but surgical treatment often causes adverse effects on the physical and mental health. Drug treatment of this disease is a hot spot of clinical research (Yu, 2018; Dai *et al.*, 2018; Jung *et al.*, 2016). Under the influence of accelerated social work and life pace, increased pressure and environmental factors, the number of women with uterine fibroids is increasing, which has become a matter of wide concern in the medical community.

Uterine fibroid is one of the most common benign tumors in the female reproductive organs, and also on

of the most common tumors in the human body, also known as fibromyoma or fibroma uteri. Uterine fibroids are mainly composed of smooth muscle cells with a small amount of fibrous connective tissue as a supporting tissue. The etiology of uterine fibroids is still not well understood, which may involve the complex interactions between normal myometrium cell mutations, sex hormones and local growth factors. According to a large number of clinical observations and experimental results, (Reiner and Robert, 2018; Li, 2016) uterine fibroids (as shown in Fig. 1) are hormone-dependent tumors. It is very important to control the disease as early as possible and improve the physical and mental health of patients. Currently, drug therapy is generally accepted as a treatment mode for patients with uterine fibroids, and cooperating with scientific nursing mode can further improve the effect of adjuvant therapy. In this study, the nursing effect the curative effects of mifepristone combined with Guizhifuling capsul in the treatment of uterine fibroids were observed and analyzed.

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Fig. 1. Color doppler ultrasonography of uterine fibroids.

MATERIALS AND METHODS

General data

In this study, 160 patients who had been treated for uterine fibroids in our hospital from October 2017 to April 2019 were enrolled as research objects. All patients had the right to know about the study and signed formal informed consent. The inclusion criteria: those having one or more tumors indicated by B ultrasound examination, with the smallest diameter of tumor above 25 mm; those having significantly increased menstrual volume, prolonged menstrual period, abdominal pain accompanied; and those who had not received treatment for uterine fibroids for recent three months. The exclusion criteria: those having poor compliance; those having serious cardiovascular and cerebrovascular diseases; those having severe mental disorders; those having drug allergies to the drug applied in this study; and those with liver abnormalities or tumors. Imaging examination of 1 patient is shown in Figure 2.

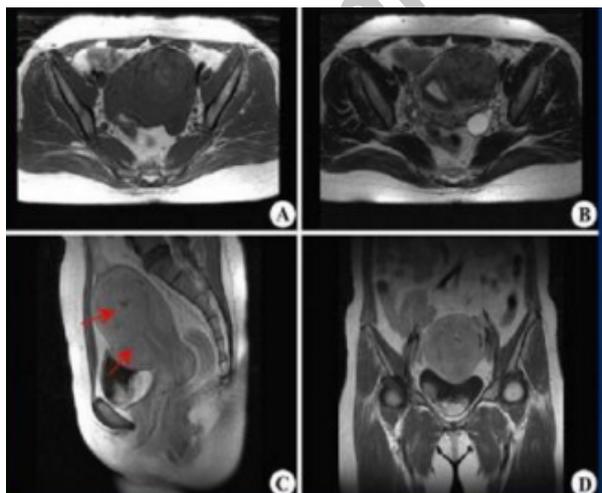


Fig. 2. MRI examination (A, B, C and D show the examination results of uterine fibroids in different directions and the disease severity increases successively from A to D).

In this study, 160 patients were randomly divided into research group and control group, each containing 80 cases. Patients in the research group ranged in age from 33 to 54 years, with an average age of (42.2 ± 2.1) years and an average course of disease of (2.5 ± 0.8) years. Patients in the control group ranged in age from 32 to 53 years, with an average age of (43.6 ± 2.8) years, and an average course of disease of (2.2 ± 0.9) years. There was no significant difference in general data between two groups before treatment, $p > 0.05$.

Medication method

Patients in the control group were routinely treated with mifepristone (Zhejiang Xianzhan Pharmaceutical Co., Ltd., SFDA approval number: H20000648), with dose of 12.5mg applied fasting state before going to bed, once a day. The medication is conducted from the day of menstruation, for 3 consecutive months as a complete course. On this basis, the patients in the research group were given Guizhifuling capsule (Jiangsu Kangyuan Pharmaceutical Co., Ltd., SFDA approval number: Z10950005), with 4 capsules for each time and 3 times a day. Similarly, the medication is conducted from the day of menstruation, for 3 consecutive months as a complete course. Mifepristone is a light yellow solid. It is not only used for resisting early pregnancy, inducing pregnancy and inducing intrauterine abortion, but also for gynecological operation, such as intrauterine iud placement and removal, endometrial specimen collection, cervical tube dysplasia laser separation, cervical dilatation and cureting. CAS No.: 84371-65-3, Molecular formula: $C_{29}H_{35}NO_2$, Molecular weight: 429.59400, Precise mass: 429.26700. To synthesize mifepristone, 4, 9 estrogens steroid diene-3,17-a ketal compound of diketone (I) were used as raw material to react with magnesium bromide of propargyne, followed by introduction of propinyl at 17 propiolic base, resulting in compound (II). Then the selective epoxidation of five olefinic bond, resulting in compounds (III). After that, tetrahydrofuran containing copper bromide-methyl sulfide complex reacts with magnesium paradimethylaminobenzene bromide, followed by introduction of p-dimethylaminophenyl at 11 propiolic base, resulting in compounds (IV). Finally, mifepristone was obtained by hydrolysis and dehydration of hydrochloric acid in In methanol, resulting in mifepristone. The yield was 21.5%. Guizhifuling capsule is a blood-regulating agent, which has the effect of activating blood circulation, removing blood stasis and eliminating disease. The contents of Guizhifuling capsule are brown fine particles, with slightly fragrant gas, slightly bitter taste. In this prescription, cassia twig warms meridians and disperses cold to activate blood circulation, tuckahoe has the function of benefiting vital energy and

support heart; danpi, peach kernel, peony have the function of promoting blood circulation to remove blood stasis.

Nursing methods

Patients in the control group were applied with general routine nursing mode, including monitoring vital signs indicators, answering questions for patients, regular rounds, etc. In contrast, patients in the research group were applied with high quality nursing on the basis of general nursing mode, including targeted health knowledge education, psychological guidance, ward environment care, dietary guidance, medication care.

Observational indices

The overall therapeutic effective rates of the two groups were compared, and three criteria were involved, including significant effectiveness, effectiveness and ineffectiveness. The therapeutic effect was evaluated by B-type ultrasonography and gynecological examination, observation of clinical manifestations, analysis of imaging data, etc. (Chen, 2017). If the clinical manifestations disappear completely or improve significantly after treatment, B-type ultrasonography indicates that the uterine fibroids disappear, or the uterine fibroids shrink by more than 50% compared with before treatment, then the standard of significant effectiveness is met. If the clinical manifestations are in good remission after treatment, b-ultrasound examination indicates that the disappearance range of uterine fibroids is 25% to 49% compared with that before treatment, then the standard of effectiveness is met. If there is no improvement before and after treatment, it is considered as ineffectiveness. In addition, the uterine volume and uterine fibroid volume before and after treatment were counted, and the incidence of adverse reactions and overall nursing satisfaction were recorded.

Statistic method

Statistical analysis software SPSS21.0 was used to process data. The measurement data were expressed by mean \pm average ($\bar{x} \pm s$), with t test conducted for intergroup comparison. Enumeration data were expressed by natural (n) and percentage (%), with chi-square used for intergroup comparison. The intergroup difference is of statistical value when $P < 0.05$.

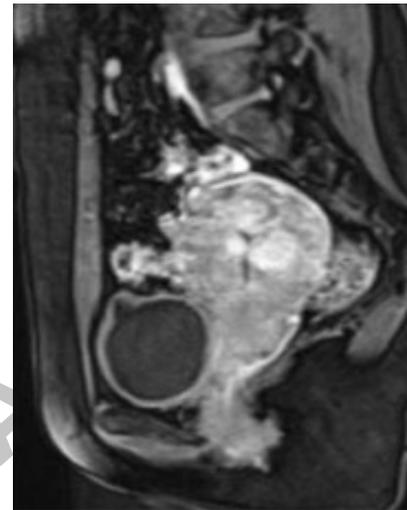
RESULTS

Comparison of the overall treatment effective rate between two groups

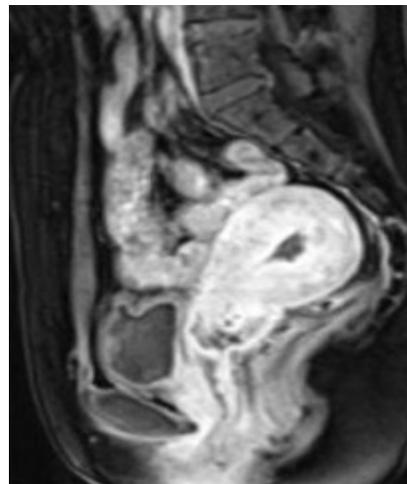
As shown in Table I below, the total effective rate of the patients in the research group was significantly higher than that of the control group, $p < 0.05$.

Comparison of uterine volume and uterine fibroid volume before and after treatment between the two groups

As shown in Table II below, the uterine volume and uterine fibroid volume in the research group showed better improvement after different treatment and nursing modes, $p < 0.05$. The examination pictures of a patient in research group before and after treatment are shown in Figure 3.



A



B

Fig. 4. Uterine volume and uterine fibroid volume are large before treatment (A) and significantly reduced after treatment (B).

Comparison of incidence of adverse reactions and overall nursing satisfaction between the two groups

As shown in Table III, compared with the control group, the incidence of adverse reactions in the research group was significantly lower, while the overall nursing satisfaction was significantly higher, $p < 0.05$.

Table I. Comparison of the overall treatment effective rate between two groups [n (%)].

Group	Number of case	Significantly effective	Effective	Ineffective	overall treatment effective rate
Research group	80	60	18	2	78(97.50)
Control group	80	28	32	20	60(75.00)
t					12.39
p					<0.05

Table II. Comparison of uterine volume and uterine fibroid volume before and after treatment between the two groups ($\bar{x}\pm s$).

Group	Uterine volume (cm ³)		Uterine fibroid volume (cm ³)	
	Before treatment	After treatment	Before treatment	After treatment
Research group (n=80)	150.49±12.48	106.26±11.84	57.66±7.60	38.59±4.31
Control group (n=80)	151.22±10.93	128.79±10.32	57.69±5.40	44.37±4.86
t	0.93	14.27	0.17	12.46
p	>0.05	<0.05	>0.05	<0.05

Table III. Comparison of incidence of adverse reactions and overall nursing satisfaction between the two groups [n (%)].

Group	Nausea and vomiting	Abdominal pain	Hot flashes	Incidence of adverse reactions (%)	Overall nursing satisfaction (%)
Research group (n=80)	2	1	2	5 (6.25)	78 (97.50)
Control group (n=80)	4	8	4	16 (20.00)	62 (77.50)
X ²				9.06	15.42
p				<0.05	<0.05

DISCUSSION

Uterine fibroids are hormone-dependent tumors. Mifepristone is a chemically synthesized steroid drug. After administration, it can well bind progesterone related receptors, inhibit progesterone activity, cause luteolysis of ovary, and weaken the contents of estrogen and progesterone receptor (Yu and Zhang, 2017; Nimdet and Techakehakij, 2017). According to related research and clinical experience, mifepristone can achieve ideal results in the treatment of uterine fibroids. However, due to individual differences of patients, some patients have poor prognosis after treatment, and corresponding auxiliary measures should be carried out. From the perspective of traditional Chinese medicine, uterine fibroids are in the category of “lump”, with emotional depression and external pathogenic factors as the pathogenesis, causing qi stagnation and blood stasis. The treatment principle is to strengthen the body and dispel evil, promote blood circulation and remove blood stasis (Kwek *et al.*, 2018). The components of Guizhifuling capsule include cassia twig, poria cocos, peach kernel and peony. The effect of

cassia twig is warming blood and toning the arteries, poria cocos exerts the effect of strengthening the spleen and dampness, the effect of peach kernel is promoting blood circulation and removing blood stasis, and Peony efficacy is removing heat to cool blood. These kinds of medicinal materials are used together to achieve the effect of activating blood circulation and removing blood stasis, exerting a better therapeutic effect. The results of this study showed that after the implementation of different treatment and nursing modes, the overall treatment effective rate of the research group (mifepristone combined with Guizhifuling capsule) was 97.50%, which was significantly higher than that (75.00%) of the control group (mifepristone alone), $p < 0.05$.

During the treatment of patients, it is necessary to cooperate with scientific nursing program, which is the key to improve the treatment effect. In this study, the high-quality nursing model was applied to the patients in the research group, and higher nursing satisfaction was obtained. The contents of high-quality nursing services are as follows. First, health publicity and education should be carried out to correct patients' wrong understanding of

the disease, improve their treatment compliance, inculcate basic knowledge and daily precautions of uterine fibroids, and actively overcome bad living habits. At the same time, patients are advised to pay attention to their own gynecological disease examination, take regular physical examination, actively prevent gynecological diseases and complications. Second, strengthen communication with patients, let them know that the treatment of uterine fibroids needs a long time, to maintain a positive and optimistic attitude, eliminate negative psychological emotions to accept the treatment, avoid unnecessary psychological burden, enhance the faith to overcome the disease. Thirdly, considering the differences in the onset and duration of different drugs as well as individual differences in patients, the nursing staff should know the best time for the administration of drugs for uterine fibroids, control the dosage of drugs, give full play to the optimal efficacy, reduce the rate of adverse reactions, and promote the recovery of the disease. Fourth, strengthen dietary guidance and environmental care. Specific and individualized dietary plans are made for patients, and patients are instructed to prohibit alcohol, avoid oily, sweet, spicy and other stimulating foods, take proper exercise. Provide patients with a warm, comfortable, clean and tidy ward environment, etc. (Ko *et al.*, 2018).

CONCLUSION

In conclusion, combined therapy of mifepristone and Guizhifuling capsule has a very significant therapeutic effect in treatment of uterine fibroids, which can significantly improve the clinical discomfort symptoms of patients, regulate the balance of hormones in patients, and has fewer adverse reactions. Moreover, this therapy is safe and reliable. On the basis of drug therapy, corresponding nursing measures, such as psychological nursing, health education, environmental nursing, are conducive to improve the treatment compliance of patients, enhance their confidence to overcome the disease, and promote the early recovery of patients' prognosis, which is worthy of clinical application.

Limitations

There are a variety of items we did not explore but could be considered for future research such as: patients' awareness about drug and data privacy policies. Better understanding of the underlying disease biology, evolution and selection, emergence of a number of effective-targeted therapies and combinations.

Statement of conflict of interest

The authors have declared no conflict of interest.

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