

# Clinical Research on Efficacy of Cassia Twig Tuckahoe Capsule and Mifepristone Combined with Laparoscopic Surgery for the Treatment of Endometriosis

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## Abstract

**Objective:** To compare the clinical efficacy of Cassia Twig Tuckahoe capsule (Chinese Medicine) and Mifepristone combined with laparoscopic surgery for the treatment of endometriosis. **Designs:** Prospective cohort study. **Setting:** Gynecology and Obstetrics Department, Jingzhou Central Hospital, affiliated to Yangtze University. **Methods:** We selected 67 patients suspected with endometriosis and divided randomly into 2 groups on patient choice. **Outcome Measures:** Treatment efficacy, side effects, recurrence rate and pregnancy rate. **Results:** Comparing the effect of treatment between the two groups, the success rate was almost same ( $P > 0.5$ ). However, the disappearance of pain was faster in Cassia twig Tuckahoe group ( $P < 0.05$ ). One patient in mifepristone group had recurrent endometriosis after 8 months from initial treatment. Comparing the side effects between the two groups, Cassia twig Tuckahoe capsule group has fewer side effects in comparison to mifepristone group. The pregnancy rate was 72% in Cassia twig Tuckahoe group while 40% in mifepristone group. **Conclusion:** After analysis of the result, Cassia twig Tuckahoe capsule combined with Laparoscopy is superior to the Mifepristone combined with Laparoscopy. Cassia twig Tuckahoe capsule is a very propitious medicine for treating endometriosis for long term benefits.

## Keywords

Cassia Twig Tuckahoe Capsule, Chocolate Cyst, Endometriosis, Laparoscopy, Mifepristone

## 1. Introduction

Endometriosis means the presence of endometrial glandular tissue outside the uterine cavity. These cells invade and proliferate locally or distantly forming functional endometriotic implants. These implants behave like normal endometrium *i.e.* they proliferate and bleed in conjunction with menstruation cycles. The exact etiology is unknown since Von Rokitonsky has proposed the term “EM” 1860 [1]. However, there are many theories explained in books and literature such as Implantation theory, Coelomic theory, Metastatic Theory and Induction Theory [2]. The most accepted theory is Implantation Theory [3]. Still research is going on to find most potent etiology such as Genetic [4], Immune Factors [5] [6], Inflammatory factors [7] [8] [9], Environment toxins [10] [11] because it occurs in certain women but not all women. Endometriosis is also considered as an estrogen dependent disorder which affects one in every ten of reproductive age.

The most common presenting symptoms are cyclical pain (dysmenorrhea), irregular bleeding, menorrhagia, dyspareunia, chronic pain (more than 6 months of non cyclic pain) and infertility [12].

The definitive diagnosis of endometriosis can only be achieved visually via laparoscopy. Although non-invasive methods for detecting endometriosis are currently under developed, such as the CA125 Antigen [13], ultrasound scanning [14], and endometrial nerve density [15], there are various methods of treatment for Endometriosis, Medical and Surgical (Open or Laparoscopy). Endometriosis is considered as an estrogen dependent disorder, therefore current medical therapies are centered upon lowering circulating estrogen levels. In western medicine, Hormone Replacement Therapy (HRT) is commonly used and it involves Oral Contraceptive Pills (OCPS), Progestogenic, Gestrinone, Danazole, GnRH agonist, but long term administration of these medicines remains challenging due to serious adverse side effects such as heavy bleeding, perimenopausal symptoms, masculinization and liver dysfunction. Instead of these side effects, data from Cleveland Clinic showed that the endometriosis recurrence rate was 20 - 40 percent within 5 years following conservative surgery, unless the patient reached menopause or hysterectomy [16]. Due to relatively poor efficacy of hormonal therapy, several other therapies for endometriosis are currently being used such as Mifepristone (a selective progesterone receptor modulator) [17], Dienogest (a progestin) [18]. The Chinese medicine has been also widely utilized since the 19<sup>th</sup> Century, and its utilization in China as well as in Western countries is increasing nowadays [19] [20]. But, still the best and effective treatment for endometriosis remains challenging. Keeping this in mind we planned to find the efficacy of Cassia twig Tuckahoe capsule (Chinese medicine) and Mifepristone combined with laparoscopy for the treatment of endometriosis.

## 2. Methods

From January 2014-March 2014, 67 patients suspected with endometriosis were

admitted to Gynecology and Obstetrics department of Jingzhou Central hospital for the treatment. The research was approved by the ethics committee of the Gynecology and Obstetrics department.

The inclusion criteria were:

- a) Patients presenting with typical symptoms indicating endometriosis.
- b) Ultrasound suspecting Endometriosis such as Presence of Chocolate cyst and Adhesions.
- c) Laboratory reports suspecting endometriosis such as raised CA125 and CRP positive.

The exclusion criteria:

- a) Laparoscopy diagnosis revealing other pathology than Endometriosis.

Therefore 8 patients out of 67 were excluded and the remaining 61 patients were divided into two groups according to their choice for Mifepristone (33 patients) and Cassia twig Tuckahoe (26 patients) and latter one patient dint come for follow up from the study group so she was also excluded. Finally 25 patients from the study group were given Cassia twig Tuckahoe capsule and 33 patients from the control group were given Mifepristone after Conservative laparoscopic management.

**Treatment:** The initial treatment for the patients in both groups was the same Conservative Laparoscopic management. Latter according to respective groups, the study group received Cassia twig Tuckahoe capsule 3 Capsule three times a day for 6 months and Control group received 10 mg 1 tablet once a day for 6 months.

**Follow up:** The patients in both groups were followed up on regular basis for a period of 1 year. The initial follow up was after 2 weeks from the day of discharge. Latter on this sedule was adjusted to once every 2 month for 6 month and then every 3 month for remaining 6 month. On every follow up following items were assessed: side effects, recurrence, menstruation cycle and pregnancy with the help of serum CA125 Antigen, Ultrasound, Clinical symptoms, Pelvic Examination, Liver function test and renal function test.

**Statistics:** The difference in categorical data between the two groups was compared using the two-sided  $X^2$  test. SPSS 12.0 Software was used and the Significant value ( $P < 0.05$ ) was considered statically significant.

### 3. Results

#### Demographic

The average age of all enrolled patient was 30 (range: 20 - 42). Out of these patients, 2 patients had previous history of endometriosis. The most common symptom with which patients presented was irregular bleeding with pelvic pain (Dysmenorrhea). The Ultrasound revealed that the average size of the cyst was 5 cm. On the day of hospitalization, 34 Patient presented with history of irregular bleeding and Dysmenorrhea, 14 patients presented with pelvic pain (Dysme-

norrhoea) only and 9 patients had regular cycle with dyspareunia. The severities of symptoms were mild in 9 patients, moderate in 14 patients and severe in 39 patients. The average duration of the symptoms among these patients was 3 months. There was no significant difference between the both group patients in any of above Demographic or clinical characteristic (**Table 1**).

#### **The efficacy, Side effects, Recurrence and pregnancy rate during 1 year follow up**

The overall success rate of the treatment between the two groups was almost same ( $P > 0.05$ ). The Serum CA125 antigen regression was not significant in our study ( $P > 0.05$ ). The average time was for Serum CA125 antigen regression was almost same. The disappearance of pain was significantly faster in the Cassia Twig Tuckahoe capsule group ( $P < 0.05$ ) in comparison to mifepristone group. The menstruation cycle normalized in more patients in Cassia twig Tuckahoe capsule group. While in mifepristone group 9 patients complaint of menorrhagia and 5 patients developed Ammenoea during the treatment but latter after completion of mifepristone course, the cycle was regular but painful (**Table 2**).

**Table 1.** Comparison of the demography and clinical characteristic between two groups.

Items	Study groups (n = 25)	Control group (n = 33)	P value
<b>Age (years)</b>			
<30	16 (64%)	21 (63.6%)	0.992
30 - 40	5 (20%)	7 (21.2%)	
>40	4 (16%)	5 (15.2%)	
<b>Previous H/O Endometriosis</b>			
NO previous history	24 (96%)	32 (97%)	0.841
Previous history	1 (4%)	1 (3%)	
<b>CA125 Antigen Level at the presentation units/ml</b>			
20 - 50	15 (60%)	15 (45.5%)	0.543
51 - 80	7 (28%)	13 (39.4%)	
>80	3 (12%)	5 (15.2%)	
<b>Diameter of endometriosis cyst on ultrasound</b>			
<2 cm	2 (8%)	3 (9.1%)	0.899
2 - 5 cm	14 (56%)	20 (60.6%)	
>5	9 (36%)	10 (30.3%)	
<b>Symptoms</b>			
Pelvic Pain + Irregular Cycle	17 (68%)	17 (51.5%)	0.316
Pelvic pain only	4 (16%)	10 (30.3)	
Irregular Cycle only	1 (4%)	0 (0%)	
Regular cycle	3 (12%)	6 (18.2%)	
<b>Severity of symptoms</b>			
Mild	5 (20%)	4 (12.1%)	0.278
Moderate	6 (24%)	4 (12.1%)	
Severe	14 (56%)	25 (75%)	

**Table 2.** Comparison of effect, side-effect, recurrence, and pregnancy outcome during 1 year follow-up.

Items	Study groups (n = 25)	Control group (n = 33)	P value
Success	25 (100%)	32 (97%)	0.380
Unsuccess	0 (0%)	1 (3%)	
<b>Duration of CA125 to normal level</b>			
<1 week	15 (60%)	15 (45.5%)	0.543
1 week-2 weeks	7 (28%)	13 (39.4%)	
>2 weeks	3 (12%)	5 (15.2%)	
<b>Disappearance of pain</b>			
<1 months	23 (92%)	18 (54.5%)	0.008
2 - 5 months	2 (8%)	13 (39.4%)	
6 - 12 months	0 (0%)	2 (6.1%)	
<b>Menstruation cycle</b>			
Normal	24 (96%)	19 (57.6%)	0.004
Menorrhagia	1 (4%)	9 (27.3%)	
Amenorrhoea	0 (0%)	5 (15.2%)	
<b>Symptoms Related to medicine</b>			
No any symptoms	19 (76%)	13 (39.4%)	0.033
Nausea	5 (20%)	12 (36.4%)	
Vomiting	1 (4%)	5 (15.2%)	
Headache	0 (0%)	3 (9.1%)	
<b>Renal Function Test</b>			
Normal	23 (92%)	32 (97%)	0.397
Dearranged	2 (8%)	1 (3%)	
<b>Liver Function Test</b>			
Normal	24 (96%)	25 (75.8%)	0.035
Dearranged	1 (4%)	8 (24.2%)	
<b>Ultrasound Reports</b>			
Normal	24 (96%)	32 (97%)	0.354
Small Collection in POD	1 (4%)	0 (0)	
Recurrence	0 (0%)	1 (3%)	
<b>Pregnancy rate</b>			
Natural Conception	9 (36%)	5 (15.2%)	0.039
In vitro fertilization	9 (36%)	8 (24.2%)	
Not Conceived	7 (28%)	20 (60.6%)	

During the follow up periods, many patients complaint Nausea and vomiting which were more prominent in mifepristone group, as a short term side effect. One patient in Cassia twig Tuckahoe capsule group and 8 patients in control group reported abnormal Liver Function Test, which shows significant between the two groups ( $P < 0.05$ ). While the renal abnormalities were not significant in our study (**Table 2**).

An ultrasound evaluation was performed for all patients. 2 weeks after the initial treatment. Among them small collection in Pouch of Douglas were found in 1 patient in the Cassia twig Tuckahoe capsule group for which one course of Metronidazole was given and it disappear at the next follow up ultrasound evaluation. 1 patient from the mifepristone group has recurrence after 8 months of initial treatment for which the patient had to go again for laparoscopic surgery for the management. She was among the 5 patient in whom Serum CA125 regress after 2 weeks.

The pregnancy rate was significant in our study ( $P < 0.5$ ). 9 patients conceived naturally and 9 patients conceive with the help of In vitro fertilization (IVF) while in mifepristone group 5 patients conceived naturally and 8 patients with the help of IVF during our study period (**Table 2**).

#### 4. Discussions

Previously Endometriosis was considered to be an estrogen dependent that affected women approaching middle age, but now it is recognized that to disease diagnosed more frequently in younger women [21]. In our study the mean age for endometriosis was 30 years. Endometriosis is not only a heavy burden for the sufferer, but also in economic terms too. The loss of work has caused by illness (severe pain, visiting clinics for treatment) due to endometriosis is estimated to the U.K. economy 2 billion pounds a year [22].

The Diagnosis of endometriosis has still not improved and usually misdiagnosed or diagnosed latter. The Definitive diagnosis of endometriosis can only be achieved visually via Laparoscopy. Although non invasive methods for detecting endometriosis are currently under developed, such as the CA125 Antigen [13], Ultrasound scanning [14], and endometrium nerve density [15]. For this reason 8 patients were excluded from our study because they had other pathology rather than endometriosis at laparoscopic management.

There is various method of treatments, medical and surgical (Open or Laparoscopy). Due to relatively poor efficacy of hormonal therapy, several other therapies such as mifepristone [17], Dienoyst [18] are used now a day. These can be used either before surgery if mild endometriosis or can be used after surgery. Many study revealed better result when combined with surgery. Now a day's Chinese medicine is gaining more popularity in china as well as in western countries with less side effect and similar success rate in comparison to mifepristone. [19]. Similarly in our study the success rate of both medicines were almost same.

The side effects that were reported after the use of each medicine were generally in the same range as those reported by other investigators [20]. One study showed that if high dose of mifepristone is given over a prolong period promotes an unopposed oestrogen milieu leading to endometrial hyperplasia, resulting in massive bleeding [23]. In our study Menorrhagia was the most prominent in mifepristone group in spite of using low dose mifepristone. The Mifepristone

have many other side effects too such as nausea, vomiting, headache, liver and renal impairment while the Cassia twig Tuckahoe does not have any such side effects other than nausea and vomiting which were also less in comparison to mifepristone. Two patients had some renal function derangement in cassia twig Tuckahoe capsule group but it may be due to diabetes because both of these patients had diabetes.

The cassia twig Tuckahoe is a very propitious medicine for dysmenorrhea as well chronic pelvic pain. One clinical trial showed that cassia twig Tuckahoe could relieve dysmenorrhea as effectively as mifepristone, with total effective rate 90% and 73% in cassia twig Tuckahoe capsule group and mifepristone groups respectively after 3 month of treatment with a study group of 120 patients [24]. Similar result was also observed with clinical trial of 42 patients treated with cassia twig Tuckahoe capsule for 6 months.

The comparison of recurrence rate in our study with those of other study is more [25]. The recurrences were more in mifepristone group. This may be due to long period of follow-up and endometrial hyperplasia leading to menorrhagia and reflux of menstruation (Implantation Theory).

In our study the overall 1 year commutative rate of pregnancy was 72% in Cassia twig Tuckahoe capsule group and 40% in mifepristone group. Cassia twig Tuckahoe is a very good for infertility treatment due to endometriosis. It normalize the menstruation cycle as well sex hormone and increase sexual desire which can increase the conception but further study on this topic is required. Other study also reported a higher pregnancy rate in Cassia twig Tuckahoe capsule group, 5 out of 10 endometriosis patients with infertility were pregnant in comparison to mifepristone [26]. Mifepristone decreases estrogen, progesterone, luteinizing hormone and makes endometrial incapable for implantation which is against pregnancy [27] [28] [29].

## 5. Conclusion

After analysis of result, Cassia twig Tuckahoe capsule combined with Laparoscopy is superior to the Mifepristone combined with Laparoscopy with regards to fewer side effects, better natural conception rate, less relapse and less menstruation disorders for the management of endometriosis. However, the success rate of both types of treatment is almost same. It should be popularized for the treatment of endometriosis for the long term patient's benefits.

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