Effect of Chinese Herbal Formula, Soothe & Shrink, on Uterine Fibroids: An Eight-Case Clinical Study

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Please see bios at end of the article.

Abstract

Objective: This study seeks to observe the effect of the Chinese herbal formula, Soothe & Shrink, on treatment of uterine fibroids.

Methods: A total of 10 participants who met the study criteria were recruited into two treatment groups, a 6-week treatment group and a 12-week treatment group, with five participants in each group. Soothe & Shrink herbal formula in granule form (10.8 g) was given to participants, taken orally twice a day. A trans-vaginal ultrasound was performed on all participants before and after treatment to evaluate uterine size and fibroid volume. Symptom severity and quality of life were also evaluated using the Uterine Fibroid Symptom and Health-Related Quality of Life Questionnaire.

Results: Two of the 6-week-group participants dropped out due to personal reasons. A total of eight participants completed the program. In six out of the eight participants, four from the 12-week group and two from the 6-week group, a reduction in uterine size was found. A higher percentage of participants in the 12-week group (four out of five, 80%) showed a reduction of uterine size than in the 6-week group (two out of three, 66.7%). In four out of the eight participants, three from the 12-week group and one from the 6-week group, a reduction in UF volume was found. A higher percentage of participants in the 12-week group (three out of five and 60%) showed a reduction in UF volume than in the 6-week group (one out of three and 33.3%). The scores for Uterine Fibroid Symptom and Health-Related Quality of Life Questionnaire showed substantial improvement in both groups. Symptom-severity subscale scores were found decreased for all participants except one. A significantly higher rate of reduction was observed for the 12-week group than the 6-week group ($p<0.01$). The quality of life subscale scores showed marked improvement for all participants except one. The increase in general quality-of-life score after treatment for the eight participants was statistically significant ($p<0.05$). The increase of the score for the 12-week group was significantly higher than that for the 6-week group ($p<0.01$).

Conclusions: The Chinese herbal formula, Soothe & Shrink, may reduce uterine size and fibroid volume as well as improve the clinical symptoms and quality of life of UF patients. A minimal treatment duration of 12 weeks may have better results than shorter treatment duration. Further clinical studies with negative controls, blinding, longer treatment duration, and larger sample size are recommended.

Keywords: Uterine fibroids, uterine fibroid symptoms and Quality of Life Questionnaire, Chinese herbal medicine, Soothe & Shrink formula

Introduction

Uterine fibroids (UFs) are benign tumors of the smooth muscle cells of the uterus.[1] UFs are among the most common diseases in women, occurring in about 25% of all women of reproductive age and up to 30–40% of women over 40 years old.[2] It is estimated that in up to 50% of the cases, UFs can cause symptoms such as excessive abdominal bleeding, abdominal pain, irregular menstruation, and infertility.[3] If left untreated, the symptoms can persist until menopause, severely impacting a woman's quality of life. UFs affect approximately 25 million women in the United States annually, with approximately six million women seeking medical treatment for severe symptoms each year.[1]

The cause of UFs remains unknown. Estrogen and progesterone receptors have been identified in fibroid tissue at levels greater than surrounding myometrial cells. It has also been recognized that fibroid growth and maintenance are stimulated and affected by hormonal cyclic changes.[1, 4]

Contemporary management of fibroids includes pharmaceutical options for the symptoms of UFs and surgical options such as hysterectomy, myomectomy, and uterine artery embolization (UAE). Pharmaceutical treatments use medications such as gonadotropin-releasing hormone (GnRH) agonists, progesterone antagonists, and female hormone replacement to relieve symptoms and decrease the growth of fibroids. The main effects of GnRH agonists, which suppress pituitary ovarian function, are the temporary control of bleeding and a reduction in fibroid and uterine size. Progesterone antagonists block progesterone signals to fibroid tissue and reduce the growth. Surgical approaches, such as hysterectomy, remain a mainstay of fibroid treatment. It is estimated that almost half of the 600,000 hysterectomies performed in the United States each year are performed to treat symptomatic UFs.[2, 4]

Current medical protocols for UFs have their limits. The side effects of GnRH agonists include menopausal symptoms and bone loss with long-term use. After therapy is stopped, there is regrowth of both the fibroids and the uterus almost to their pre-treatment size and a recurrence of symptoms in most patients.[2] Progesterone antagonists and other hormonal therapies that alter estrogen and progesterone production or function may lead to further hormonal imbalance. The surgical approach is associated with operative mortality and morbidity. These medical and hormonal therapies also have critical shortcomings such as causing menopausal syndrome and infertilities.[2, 5, 6] Thus, safer therapies are needed for clinical management of UFs.

In China, traditional Chinese medicine (TCM) is a common treatment for UFs. TCM categorizes UFs as *zhen jia*, "the agglomeration/lumps in lower abdomen, accompanied with pain, distending or bloating sensation, and even bleeding."[7] The etiology of this condition is related to *qi* deficiency and disharmony between *qi* and Blood, and in most cases, agglomeration occurs due to *qi* stagnation and Blood stasis with Dampness and Phlegm accumulation in the Interior.[7]

Gui Zhi Fu Ling Wan (Cinnamon and Poria Pill) is one such common herbal formula for this condition.[8] First described in *Jin Gui Yao Lue* (Essential Prescriptions from the Golden Cabinet) by famous TCM doctor Zhang Zhong Jing of the Han Dynasty (third century A.D.), the formula consists of five herbs: *gui zhi* (Ramulus Cinnamomi), *fu ling* (Poria), *tao ren* (Semen Persicae), *chi shao* (Radix Paeoniae rubra) or *bai shao* (Radix Paeoniae alba), and *dan pi* (Cortex Moutan). The functions of this formula include invigorating Blood, dissolving stasis, and resolving masses.[9] Studies found that *Gui Zhi Fu Ling Wan* may help the shrinkage of UFs and could be an alternative to drug therapies and surgery.[5] However, the effectiveness of the formula is still controversial due to an insufficient number of studies utilizing large sample sizes and commonly accepted standards in research methodology.[10]

Gui Zhi Fu Ling Wan has been researched on therapeutic mechanisms for various conditions. It has been reported that the formula helped hot flashes through modulating peripheral blood circulation. Studies found that blood flow in the face and upper body decreased significantly with both estrogen and *Gui Zhi Fu Ling Wan* treatment. But the herbal formula significantly increased the blood flow in the lower extremities, whereas estrogen decreased the blood flow.[11] *Gui Zhi Fu Ling Wan* has also been reported to induce apoptosis of endometriotic cells and inhibit cell proliferation and metastasis through the mitochondrial apoptotic pathway.[12] In addition, both in vitro and in vivo studies found that *Gui Zhi Fu Ling Wan* had anti-tumor function with inhibition of growth and angiopoiesis of human cervical cancer cells.[13] Thus, it is reasonable to believe that *Gui Zhi Fu Ling Wan* reduces UF through similar pathways. However, detailed therapeutic mechanisms remain unclear.

In addition to the symptoms directly associated with UFs such as irregular menstruation, menorrhagia, pelvic pain and discomfort, many other symptoms have also been observed among UF patients. These include anxiousness, fatigue, mood change, worry, and low sex drive.[14] Considering that nowadays working women must cope with high stress in balancing their careers and families, the above symptoms further reduce their quality of life.

Many Chinese herbs have been studied and found beneficial in treating the above symptoms. *Chai hu* (Radix Bupleuri), *bai shao* (Radix Paeoniae alba), and *dang gui* (Radix Angelicae sinensis)—major ingredients of the classical formula *Xiao Yao Wan* (Free and Easy Wanderer)—have been found to reduce psychological stress, as well as the negative emotions of depression and/or anxiety. It is suggested that *Xiao Yao Wan* regulates nervous and endocrine systems through enhancing levels of plasma β-endorphins and decreasing epinephrine and dopamine release.[15] Furthermore, *dang gui* (Radix Angelicae sinensis) has been found to have estrogen receptor binding activity and to promote progesterone receptor gene expression in vitro.[16] Clinical studies have also reported that *dang gui* can ameliorate the symptoms of menopausal syndrome and helps related physical and psychological symptoms.[17] Study suggests that *dang gui* may modulate estrogen receptor function through activation of estrogen receptor signaling pathways.[16] Thus, it is reasonable to believe that this herb may also help decrease the growth of UFs.

San qi (Panax notoginseng) is another widely used Chinese herb that has wide-ranging pharmacological effects and can be used to treat cardiovascular diseases, pain, inflammation, and internal and external bleeding. Study suggests that the herb helps to stop bleeding and speed up wound healing through enhancing platelet aggregation via activating signaling pathways.[18] Although *San qi* (Panax notoginseng) is often used to stop bleeding caused by trauma, according to TCM theory, its dual-functions, stopping bleeding and moving stasis, suggest that this herb could also be a good choice to treat UFs and related symptoms.

For the purpose of this study, the authors designed an herbal formula to treat UFs, Soothe & Shrink (S&S) formula, based on modern research and traditional formulation strategy. This formula uses a combination of *Gui Zhi Fu Ling Wan, Xiao Yao Wan,* and other Chinese herbs, including *fa ban xia* (Processed Rhizoma Pinelliae Ternatae), *shan zha* (Crataegi Fructus), *xiang fu* (Cyperus Rhizome), *yi mu cao* (Herba leonuri), *ju he* (Semen Citri reticulatae), *san qi* (Radix Notoginseng), and *jiu chao da huang* (Wine Processed Radix et Rhizoma rhei). The objective of the study is to determine the therapeutic effect of the S&S formula in reducing uterine size and UF volume as well as controlling related clinical symptoms.

Materials and Methods

The study design and treatment protocol were reviewed and approved by the Atlantic Institute of Oriental Medicine Institutional Review Board. The study was conducted by a licensed acupuncturist in a private acupuncture clinic. Participants were recruited through digital and print advertisements. Ten participants were enrolled in the study using the diagnostic criteria shown in Table 1. The participants were divided into two groups, with the first five in the 12-week group and the latter five in the 6-week group. All participants were provided with written informed consent before the study and a list of board-certified physicians in the event that they experienced psychologically, emotionally, or physically adverse effects during the study.

Table 1. Diagnostic, Inclusion, Exclusion and Dropout Criteria

Diagnostic Criteria	1. Primary complaint includes one or more of the followings: • Heavy or prolonged menstrual periods • Abnormal bleeding between menstrual periods • Pelvic pain (caused as the tumor presses on pelvic organs) • Frequent urination • Low back pain • Pain during intercourse • A firm mass, often located near the middle of the pelvis, can be felt by a physician 2. In addition to 1 above, diagnosis of UF must be confirmed with physical examination by a physician and with transvaginal ultrasound (also known as ultrasonography).
Inclusion Criteria	1. Met the diagnostic criteria described above for UF 2. Were between 25 and 51 years old 3. Were at pre-menopause stage 4. Had fewer than 4 missed periods within the past year 5. Signed Informed Consent and Release of Liability Forms 6. Were reported to have one or more of the fibroids equal or smaller than 1.97 x 1.97 x 1.97 cubic inches or 5 x 5 x 5 cubic centimeters 7. Received a minimum of junior high school education 8. Read the provided list of the formula's ingredients to ensure no known allergies
Exclusion Criteria	1. Used one or more of the UF interventions including Gonadotropin-releasing hormone agonists (GnRH agonists), anti-hormonal agents, and anti-progestin one month before the study 2. Had myomectomy and/or uterine artery embolization done within 6 months 3. Experienced excessive uterine bleeding with one or more of the following symptoms: a. A need to use double the amount of feminine hygiene products typically used and having to change them during the night, or use protective barriers on the bed b. Menstrual bleeding extended to more than 10 days 3 months prior to the study 4. Anemia or signs of abnormal functions of liver and kidney using complete blood count (CBC) and comprehensive metabolic panel (CMP)
Dropout Criteria	Missed more than 3 consecutive days of taking herbal formula

The ingredients of the S&S formula and daily dosage are shown in Table 2. Herbal extracts were manufactured by Beijing Kang Ren Tang Pharmaceutical Co. and sponsored by Acupuncture Corporation of America, New York. Participants were instructed to take one dose of herbal extract (10.8 g) twice a day, half an hour after breakfast and half an hour after dinner. The extract was dissolved in hot water of 88-100 C by stirring and cooled down for about two minutes before taking. Stevia extract (1 g) and lemon juice powder (5 g) were available upon request for patients who experienced difficulties in drinking the decoction. Herbs were skipped during menstruation. Weekly interviews were scheduled with the participants. During the interview, 1) the implement of the study procedure was monitored; 2) general health conditions of participants were assessed with a pulse and tongue read; 3) questions and concerns from the participants were discussed; and 4) one week of herbs were given to the participants. No nutritional or lifestyle changes were recommended and no additional modalities of treatment were used.

Table 2. Ingredients of S&S Formula and Daily Dosage

Name of Herbs	Ratio (Extract vs. Raw Herb)	Raw Herb Dosage (g)	Exact Dosage (g)
gui zhi (Ramulus Cinnamomi cassiae)	1:20	10	0.5
fu ling (Sclerotium Poriae cocos.)	1:5	10	2
bei chai hu (Radix Bupleuri)	1:10	10	1
huang qin (Radix Scutellariae baicalensis)	1:10	7	0.7
dan pi (Cortex Moutan Radicis)	1:10	10	1
chi shao (Radix Paeoniae Lactiflorae)	1:10	10	1
tao ren (Semen Persicae)	1:20	10	0.5
fa ban xia (Processed Rhizoma Pinelliae Ternatae)	1:10	8	0.8
shan zha (Crataegi Fructus)	1:5	10	2
xiang fu (Cyperus Rhizome)	1:20	7	0.35
yi mu cao (Herba leonuri)	1:10	7	0.7
ju he (Semen Citri reticulatae)	1:20	5	0.25
san qi (Radix Notoginseng)	1:1	8	8
jiu chao da huang (Wine Processed Radix et Rhizoma rhei)	1:20	8	0.4
dang gui (Radix Angelicae sinensis)	1:5	7	1.4
gan cao (Radix Glycyrrhizae uralensis)	1:5	5	1
Total		132	21.6

The primary outcome measurements of this study, uterine size, UF volume, and number of UFs, were evaluated with transvaginal ultrasounds performed by the Flushing Imaging Center, New York. Both the volume of the UFs and/or the volume of uterine were calculated by the Prolate Ellipsoid Method, via the formula: $0.52 \times \text{length} \times \text{width} \times \text{height}$.[2] All participants received a transvaginal ultrasound before and after the treatment at around 10 days after the first day of the participants' menstrual period.

The secondary outcome measurement of this study, i.e., the symptoms and quality of life, were evaluated using a modified version of the "Uterine Fibroid Symptom and Quality of Life Questionnaire (UFS-QOL)."[14,19] The UFS-QOL is a UF-specific questionnaire that assesses symptom severity and the quality of life in patients with uterine fibroids. It consists of an 8-point Symptom Severity scale questionnaire and 29 Quality of Life questions comprising six areas: concern (about unpredictability of the menstruation and embarrassment caused by heavy bleeding), activities (daily physical activities and exercise), energy/mood (energy level and mood change), control (feelings of lost control of own life, health, and mood), self-consciousness (about appearance, weight, and size of cloth), and sexual function (sexual desire and relations). All questions are scored on a 5-point Likert scale, ranging from "not at all" to "a very great deal" for symptom severity questions and "none of the time" to "all of the time" for the quality-of-life questions. Symptom Severity and Quality-of-Life subscale scores are summed into a 0–100 point scale. The Symptom Severity scale and Quality-of-Life subscale scores are inversely related with higher Symptom Severity scores, indicating greater symptoms, while higher Quality-of-Life subscale scores indicate better quality of life.[19]

The UFS-QOL has been used in a number of studies assessing a variety of UF therapies,[20-22] and has been found to be a useful outcome measurement for UF treatment.[19] The original UFS-QOL questionnaire consisted of 37 questions. Three additional questions were added to the end of the questionnaire to further evaluate the severity of the irregular menstruation, abdominal pain, and trouble sleeping. The questions added are: "(38) Fluctuation in your irregular menstrual cycle;" "(39) Abdominal pain of your periods;" and "(40) Interfered with your sleeping." The UFS-QOL was given to each participant before treatment to establish a baseline, and then administered at the end of the study. The scores collected were entered into a Microsoft Excel spreadsheet for comparison and statistical analysis.

The Complete Blood Count (CBC) and Complete Metabolic Panel (CMP) were conducted before and after the study to check for anemia and liver and kidney function and to ensure that the participants would not be adversely affected during the course of the study.

Results

1. Baseline Demographics

Among the 10 participants who completed the baseline UFS-QOL and received initial UF treatment, five of the five participants in the 12-week group completed the treatment and three of the five participants in the 6-week group finished the treatment. Two participants of the 6-week group did not finish the treatment due to personal reasons, resulting in a total sample size of eight participants. Among the eight participants, ages ranged from 35 to 51, with a mean age of 45 years old. Seven participants were Asian and one was Caucasian, with a mean body mass index (BMI) of 23.3 (Table 3). Each participant received a patient code based on the number of weeks they participated (e.g. those in the 12-week group have number "12" in their codes, while those in the 6-week group have a number "6" in their codes) and their name initials.

Table 3: Baseline Demographic and Clinical Characteristics

Patient Code	Body Weight (lb)	Height	BMI*	Age	Race
PT12ACN	120	5'3''	21.3	49	Asian
PT12BWX	115	5'1''	21.7	46	Asian
PT12CXJ	120	5'5''	20.0	48	Asian
PT12DWL	140	5'1''	26.5	35	Asian
PT12ECD	153	5'3''	27.1	44	Asian
PT06AWM	170	5'10''	24.4	47	Asian
PT06BDX	130	5'2''	23.8	37	Asian
PT06CAT	115	5'1''	21.7	51	Caucasian
Mean	132.9	5'3''	23.3	44.6	Asian=7; Caucasian=1

*BMI-body mass index

2. Change of Uterine Size

Among the eight participants who finished the program, six showed a reduction in uterine size, while one participant (PT06BDX) in the 6-week group showed an increase and one (PT12DWL) in the 12-week group showed no change. A higher percentage of participants in the 12-week group (4 out of 5, 80%) showed a reduction of uterine size than in the 6-week group (2 out of 3, 66.7%) (Table 4). No statistically significant change in uterine size was observed before and after treatment among the eight participants.

3. Volume of UFs

Four out of eight participants showed a reduction in UF volume. In the 12-week group, three out of the five participants showed a reduction, while one participant (PT12BWX) showed an increase and the other (PT12ACN) showed no change. In the 6-week group, one out of three participants showed a reduction in UF volume, while the other two participants (PT12BWX and PT06CAT) showed an increase (Table 4). A higher percentage of participants in the 12-week group (three out of five and 60%) showed a reduction in UF volume than in the 6-week group (one out of three and 33.3%). No statistically significant change in UF volume was observed before and after treatment among the eight participants

4. Number of UFs

A decrease in number of fibroids was observed in two participants (PT12CXJ and PT12DWL) in the 12-week group and one (PT06BDX) in the 6-week group. Two participants (PT12ACN and PT12BWX) in the 12-week group and 1 (PT06AWM) in the 6-week group showed no change in number of fibroids, while 2 participants (PT12ECD and PT06CAT), one in each group, showed an increase in number of fibroids (Table 4). There was no statistically significant change in number of fibroids before and after treatment among the eight participants, nor were there between the two groups.

Table 4. Change in Uterus Size, Fibroid Volume, and Number of Fibroids

Patient Code	Uterus Size			Fibroid Volume			Number of Fibroids		
	Before (cm^3)	After (cm^3)	Change (%)	Before (cm^3)	After (cm^3)	Change (%)	Before	After	Change
PT12ACN	102.1	44.2	-56.71	520.0	520.0	0	1	1	0
PT12BWX	212.4	128.8	-39.36	49.7	62.3	+25.35	2	2	0
PT12CXJ	1630.6	735.9	-54.87	1270.7	924.0	-27.28	10	7	-3
PT12DWL	73.6	74.1	+0.68	26.3	13.0	-50.57	3	2	-1
PT12ECD	500.8	186.1	-62.84	231.4	119.5	-48.36	1	3	+2
PT06AWM	295.7	116.8	-60.50	289.0	355.3	+22.94	3	3	0
PT06BDX	500.4	687.1	+37.31	319.9	233.0	-27.16	2	1	-1
PT06CAT	118.2	89.2	-24.53	1.1	18.5	+1581.82	1	3	+2

"Results suggest that S&S formula is an effective treatment for UFs through reducing uterine size and UF volume and through improving symptoms and quality of life for UF patients."

5. UFS-QOL Symptom Severity

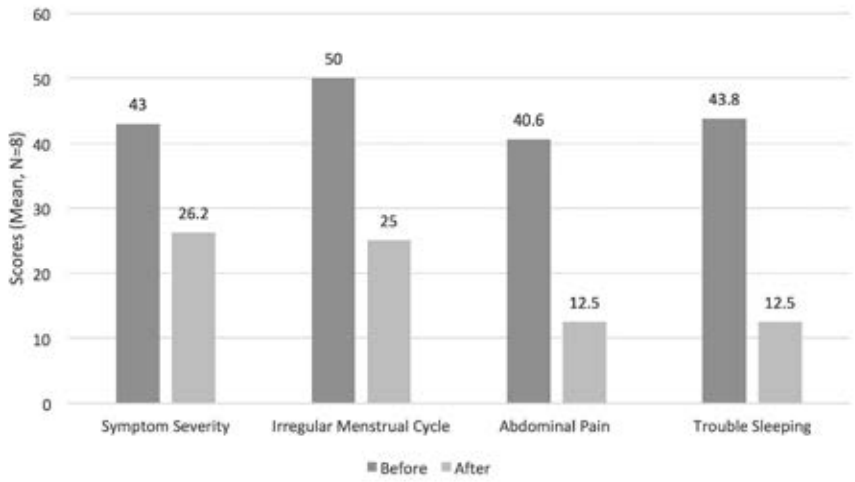
UFS-QOL Symptom Severity scores and the three additional scores for irregular menstruation, abdominal pain, and sleeping disturbance were reduced for all participants except for one, PT06AWM, who showed an increase in all scores but one, a mild reduction (33.3%) in trouble sleeping. The average scores before and after treatment are shown in Table 5 and Figure 1 and further compared between the 12-week and the 6-week groups in Figure 2. A statistically significant higher rate of symptom reduction, $t(6)=4.33$, $p<0.01$, was observed for the 12-week than the 6-week group.

Table 5. UFS-QOL Subscale Scores of Symptom Severity

UFS-QOL Subscales	6-Week Group (N=3)			12-Week Group (n=5)			Both Groups (N=8)		
	Before Mean (SD)	After Mean (SD)	Decrease (%)	Before Mean (SD)	After Mean (SD)	Decrease (%)	Before Mean (SD)	After Mean (SD)	Decrease (%)
Symptom Severity	40.6 (6.8)	37.5 (15.5)	7.6	44.4 (27.9)	19.4 (10.3)	56.3	43.0 (22.5)	26.2 (15.3)	39.0
Irregular menstrual Cycle	58.3 (23.6)	50.0 (35.4)	14.2	45.0 (29.2)	10.0 (12.2)	77.8	50.0 (28.0)	25.0 (30.6)	50.0
Abdominal pain	33.3 (11.8)	33.3 (47.1)	0.0	45.0 (40)	0.0 (0)	100.0	40.6 (32.9)	12.5 (33.1)	69.2
Trouble Sleeping	50.0 (20.4)	25.0 (20.4)	50.0	40.0 (40.6)	5.0 (10)	87.5	43.8 (34.8)	12.5 (17.7)	71.5

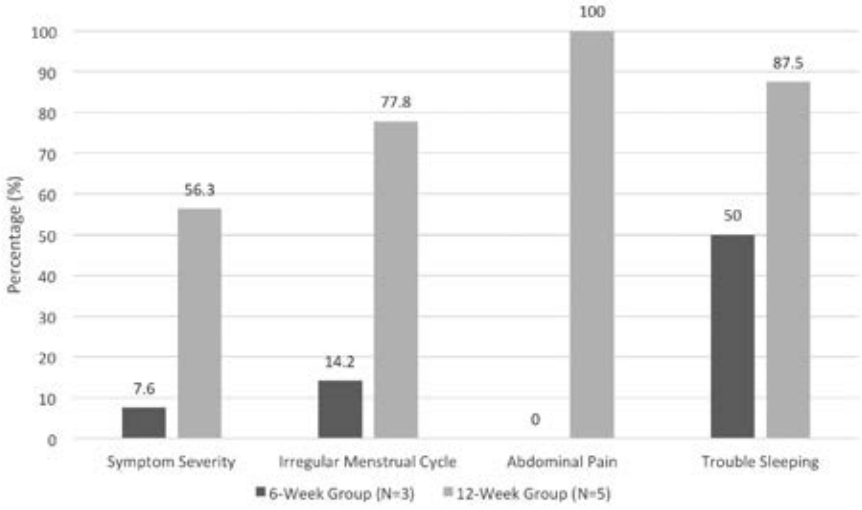
Abbreviations: SD-standard deviation; UFS-QOL-Uterine Fibroid Symptom and Quality of Life Questionnaire

Figure 1. Changes in Symptom Severity Scores before and after Treatment



Changes in symptom severity scores and the three additional scores, means of the 8 participants, were plotted to compare before and after treatment.

Figure 2. Decrease in Symptom Severity Scores between Two Groups

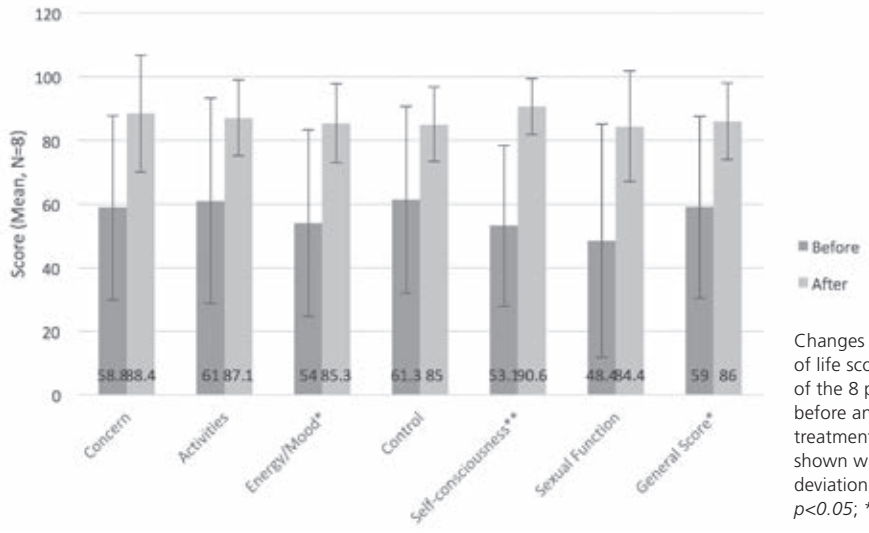


Percentage decrease in the symptom severity scores and the three additional scores were shown to compare the difference between the 6-week group and the 12-week group.

6. UFS-QOL Quality of Life

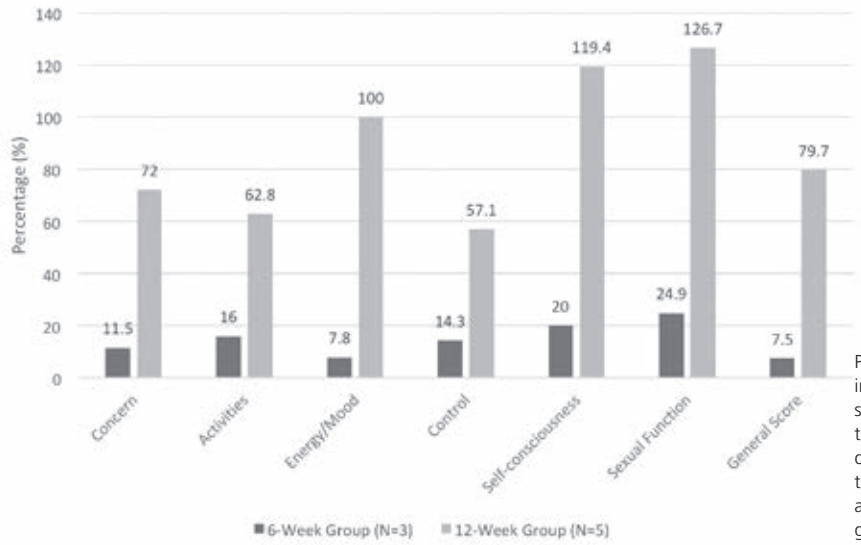
UFS-QOL Quality of Life scores for all subscales including concern, activities, energy/mood, control, self-consciousness, and sexual function increased for all participants with one exception, PT06AWM, who showed a slight decrease in all categories. The average scores before and after treatment are shown in Table 6 and Figure 3 and further compared between the 6-week and 12-week groups in Figure 4. There is significant change for the UFS-QOL General score, $t(9) = -2.29$, $p<0.05$, with the patients reporting higher scores after treatment than before treatment. This indicates that the increase of overall UFS-QOL score is statistically significant. There were also significant effects for the subscale scores of energy/mood and self-consciousness, $t(9) = -2.59$, $p<0.05$ and $t(9) = -3.70$, $p<0.01$, respectively, with higher scores after treatment than before treatment. This indicates that the increase in these scores after treatment is statistically significant. A statistically significant higher rate of increase in the scores for the 12-week group than the 6-week group was also observed, $t(5)=5.94$, $p<0.01$.

Figure 3. Changes in Quality of Life Score before and after Treatment



Changes in quality of life scores, means of the 8 participants, before and after treatment, were shown with standard deviation indicated. *- $p<0.05$; **- $p<0.01$.

Figure 4. Increase in Quality of Life Scores between Two Groups



Percentage increase in quality of life scores were shown to compare the difference between the 6-week group and the 12-week group.

Table 6. UFS-QOL Subscale Scores of Quality of Life

UFS-QOL Subscales	6-Week Group (N=3)			12-Week Group (n=5)			Both Groups (N=8)		
	Before Mean (SD)	After Mean (SD)	Increase (%)	Before Mean (SD)	After Mean (SD)	Increase (%)	Before Mean (SD)	After Mean (SD)	Increase (%)
Concern	73.3(16.5)	81.7(19.3)	11.5	50.0(31.3)	86.0(17.4)	72.0	58.8(29.0)	84.4(18.3)	43.5
Activities	69.8(21.2)	81.0(12.1)	16.0	55.7(36.5)	90.7(10.3)	62.8	61.0(32.3)	87.1(12.0)	42.8
Energy/Mood	69.0(6.7)	77.4(12.1)	7.8	45.0(33.7)	90.0(9.9)1	100.0	54.0(29.4)	85.3(12.4)1	58.0
Control	70.0(12.2)	80.0(10.8)	14.3	56.0(35.0)	88.0(11.2)	57.1	61.3(29.4)	85.0(11.7)	38.7
Self-Consciousness	69.4(19.6)	83.3(6.8)	20.0	43.3(23.2)	95.0(6.7)2	119.4	53.1(25.3)	90.6(8.8)2	70.6
Sexual Function	66.7(31.2)	83.3(11.8)	24.9	37.5(35.4)	85.0(20)1	126.7	48.4(36.7)	84.4(17.4)	74.4
General Score	74.6(9.9)	80.5(11.4)	7.5	49.7(32.1)	89.3(11.2)1	79.7	59.0(28.7)	86.0(12.1)1	45.8

1-P≤0.05; 2-P≤0.01 Abbreviations: SD-standard deviation; UFS-QOL-Uterine Fibroid Symptom and Quality of Life Questionnaire.

7. Side Effect and Safety Assessment

There were no reports on any side effect of the S&S formula based on clinical observation. Pre- and post-treatment blood work, including CBC and CMP, were conducted to check for anemia and liver and kidney functions. No participants were adversely affected during the course of the study.

Discussion

Primary outcome measurement of the study shows a reduction of uterine size in six out of eight participants and a reduction of UF volume in four out of eight participants. The reduction is not statistically significant, probably due to the small sample size of the study. Secondary outcome measurement with the questionnaires also indicates that all but one participant improved on the UF Symptom Severity and Quality of Life scales. The improvement for General Quality of Life score and subscale scores of Energy/Mood and Self-Consciousness is statistically significant. No obvious side effects were observed after 12 weeks of treatment. Results suggest that S&S formula is an effective treatment for UFs through reducing uterine size and UF volume and through improving symptoms and quality of life for UF patients. It also indicates that the S&S formula may be a safe and promising alternative to hormonal therapy and surgery to UF patients.

The results also indicate that the 12-week protocol works better than the 6-week one in terms of reduction of uterine size and UF volume, as well as symptom management. Uterine size generally reduced within six weeks, but UF volume didn't, which suggests that different mechanisms may be involved in reduction of uterine size and UF volume. Nevertheless, increase in treatment time very likely helps in the reduction of uterine size and UF volume and the management of clinical symptoms.

The limitations of this pilot study include its small sample size and the lack of negative controls. Future studies with standard design are needed to verify the result. Treatment longer than 12 weeks, e.g. 4-6 months, should be considered in the future studies. A 3-month follow-up after treatment is also needed to evaluate long-term effect of the formula.

The S&S formula used in the study is designed based on TCM patterns of *qi* stagnation and Blood stasis with Dampness and Phlegm. In the study, no further pattern differentiation was conducted for each patient. Improvement has been found for most of the patients, suggesting that the formula works for majority of the UF patients. However, detailed pattern differentiation for each patient and individualized modification to the S&S formula may still help to improve efficacy of this formula in everyday clinical practice.

"One of the difficulties in conducting clinical studies with Chinese herbs is finding ways to help participants overcome the taste of the herbs. Taste was one of the reasons cited by the two participants for the decision to discontinue participation in the study."

This study didn't give any nutritional and lifestyle recommendations and ensured that the participants continued whatever they had already been doing in terms of diet and lifestyle. However, dietary and lifestyle change is very important in TCM therapies. For the condition of UFs, *qi* stagnation and Blood stasis with Dampness and Phlegm accumulation, it is recommended that patients avoid consuming crab, shrimp, sea cucumbers, royal jelly, and e *jiao* (Colla Corii Asini, Donkey-Hide Gelatin) in their diet. These foods and supplements may promote Dampness and Phlegm and worsen *qi* stagnation and Blood stasis. In fact, some the participants in this study did consume these regularly, which likely interfered with the treatment of the S&S formula. To achieve the best clinical outcomes, dietary recommendation is a must in clinical practice.

One of the difficulties in conducting clinical studies with Chinese herbs is finding ways to help participants overcome the taste of the herbs. Taste was one of the reasons cited by the two participants for the decision to discontinue participation in the study. In fact, drinking herbal decoctions for more than one month has always been an issue for patients in daily clinical practice. By adding lemon juice powder and stevia leaf powder to the herbal granule decoction, seven out of eight participants reported that the taste of the decoction improved significantly and became more tolerable. Thus, lemon juice and stevia extract may be helpful in clinical practice as well as clinical studies involving Chinese herbal decoction.

Conclusion

Although conducted with a small sample size and lack of negative controls, this pilot study found that S&S formula was an effective treatment and safe alternative to drugs and surgery for UF patients. The formula helps UF patients by reducing uterine size and UF volume and by improving symptom severity and quality of life with a minimum of 12 weeks of continuous treatment. Further clinical studies with longer treatment durations, larger sample size, and randomized controls are warranted.

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Conflict of Interests

There are no conflicts of interest in this study.

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