Introduction

Recurrent miscarriage refers to 3 or more spontaneous miscarriages within 28 weeks of pregnancy. It is a common complication of pregnancy, with a 5% incidence rate. Recurrent miscarriage is a complex process caused by one or more factors such as genital malformations, genetic factors, immune dysfunction, endocrine abnormalities, infection factors and so on. Recurrent miscarriage increases the psychological burden of patients and causes negative psychological adverse events such as anxiety, fear, tension and depression, and can even induce spontaneous abortion. At present, there is no effective method for clinical treatment of recurrent miscarriage complicated by anxiety and depression. Western medicine often uses psychological intervention and supplementation of exogenous progesterone levels to treat these patients. Psychological interventions include supportive therapy, cognitive therapy, psychological counseling, etc., which can help patients alleviate negative psychology, but it is difficult to achieve satisfactory results. When treated with exogenous progesterone, adverse events such as skin allergy and pain at the injection site may occur in some patients, which may affect the patients’ satisfaction level. Therefore, how to effectively treat patients with recurrent miscarriage combined with anxiety and depression is the top priority of clinical research at this stage.

In recent years, with the continuous expansion of traditional Chinese medicine (TCM), plentiful experience in the treatment of recurrent miscarriage with anxiety and depression is the top priority of clinical research at this stage. Western medicine often uses psychological intervention and supplementation of exogenous progesterone levels to treat these patients. Psychological interventions include supportive therapy, cognitive therapy, psychological counseling, etc., which can help patients alleviate negative psychology, but it is difficult to achieve satisfactory results. When treated with exogenous progesterone, adverse events such as skin allergy and pain at the injection site may occur in some patients, which may affect the patients’ satisfaction level. Therefore, how to effectively treat patients with recurrent miscarriage combined with anxiety and depression is the top priority of clinical research at this stage.

Methods

From December 2016 to December 2019, 100 patients with recurrent miscarriage complicated by anxiety and depression were enrolled in our study, and a prospective randomized trial was carried out. Patients were randomly assigned to either the control group or the BSSG group via the random number table method. Traditional Chinese medicine (TCM) syndrome scores, laboratory indicators and psychological changes were compared in the two groups before and after treatment.

Results

After treatment, the primary, secondary and total TCM syndrome scores in the two groups were lower, and the scores in the BSSG group were significantly lower than in the control group. The clinical curative effect in the BSSG group was significantly higher (92% vs 76%) than in the control group. The levels of β-HCG, P, E2 and AT-III in the two groups were higher, while levels of D-D, platelet aggregation rate and Hcy were lower than before treatment. The Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS) scores were lower after treatment in both groups, and the scores in the BSSG group were significantly lower than in the control group.

Conclusions

The BSSG method may be worthy of consideration because it improves pregnancy outcomes in patients with recurrent miscarriage complicated by anxiety and depression. (Altern Ther Health Med. 2022;28(6):124-131)
depression has been accumulated. Therefore, based on more than 10 years of clinical experience, the author (Rong Cang) developed the Bushen-Shugan (BSSG) method based on the warming yang and resolving turbid method taught by teacher Xia Tian, which has the effect of nourishing the blood and tonifying the kidneys, calming the mind and regulating emotions. Thus, this study aimed to explore the effects of using the BSSG method on pregnancy outcome, serum D-dimer (D-D), platelet aggregation rate, homocysteine (Hcy) and antithrombin III (AT-III) in patients with recurrent miscarriage complicated by anxiety and depression.

Patients

From December 2016 to December 2019, 100 patients with recurrent miscarriage combined with anxiety and depression who were diagnosed and treated at the Shijiazhuang Maternity Hospital in China were included in this prospective randomized controlled study. The patients were randomly assigned to either the control group (n = 50; treated with Western medicine) or the BSSG group (n = 50; treated with the BSSG method on the basis of the control group) via the random number table method. There was no significant difference in general data between the 2 groups (P > .05), as shown in Table 1.

The study was approved by the Ethics Committee of The Fourth Hospital of Shijiazhuang (No. 20200059). All patients and their families voluntarily participated in the study and signed an informed consent form, and the formulation of this study program was in line with the relevant requirements of the Helsinki Declaration of the World Medical Association.

Diagnostic Criteria

TCM diagnostic criteria. According to Gynecology of Traditional Chinese Medicine, the diagnostic criteria for recurrent miscarriage with kidney deficiency and liver depression combined with anxiety and depression are established. Main symptoms: repeated pregnancy and fall, a small amount of vaginal bleeding, light and clear in color; lower abdomen pain, back pain, breast pain on both sides; anorexia. Secondary symptoms: sigh, or emotional depression or irritability; dizziness, tinnitus; tongue and pulse: red tongue, little coating, slippery pulse string.

Western medicine diagnostic criteria. According to the 2016 version of the Expert Consensus on the Diagnosis and Treatment of Recurrent Abortion, the diagnostic criteria for recurrent miscarriage combined with anxiety and depression are: the fetus is lost ≥3 times before 28 weeks gestation and a Self-rating Anxiety Scale (SAS) score ≥50 points and the Self-Rating Depression Scale (SDS) >53 points.

Inclusion Criteria

Patients: (1) conformed to the diagnostic criteria of TCM and Western medicine; (2) in whom both husband and wife had normal chromosomes; (3) with normal mental health and cognitive function; (4) with an SAS score of 50 to 70 points; (5) with an SDS score of 54 to 72 points; (6) not taking antipsychotic medications; (7) with normal thyroid function; (8) with normal autoimmune antibodies; (9) with no genital tract infections; (11) not taking hormone or anticoagulant drugs for the past month.

Exclusion Criteria

Patients: (1) in whom the husband or wife had a genetic disease; (2) with male azoosperma; (3) who had reproductive tract malformation or uterine fibroids, ovarian cysts and other diseases; (4) had Rh or ABO blood type incompatibility between the couple; (5) who were allergic to the study drug; (6) had abnormal liver or kidney function; (7) had neurological disease; (8) had serious adverse reactions to the study drugs.

METHODS

All patients began drug treatment from the date of diagnosis of intrauterine pregnancy. The choice of Western medicine treatment and BSSG treatment in the 2 groups was determined according to disease severity. The BSSG group was treated with TCM until 14 weeks of pregnancy. All patients received psychological intervention: A psychological intervention team was set up, which was composed of a TCM attending physician, an obstetrics and gynecology attending physician, a psychologist, a head nurse and 2 competent nurses, to carry out targeted mental health education for the patients for 14 weeks.
Scale (HAM-D) scores, the intervention team actively communicated with and helped the patients grasp and cope with their psychological state. After psychological intervention, the nurses explained the symptoms of anxiety and depression during pregnancy to the patients’ families, how to correctly deal with them and established psychological defense mechanisms and family health education. Each participant was tested after psychological counseling to evaluate the effect of psychological support. The psychological intervention team organized mental health education sessions twice a month, and the patients needed to be accompanied by their families. Each time, experts in the field and patients with a good recovery were invited to communicate on the spot, and patients were encouraged to communicate with each other.

**Western Medicine Treatment**
In addition to the psychological intervention, the control group received routine Western medicine treatment as follows:

1. Dydrogesterone (approval number: H20170221; Abbott Biologicals B.V. [Holland]), 10 mg 3 times/day (TID) up until 12 to 14 weeks gestation
2. In patients with thrombotic syndrome, oral aspirin enteric-coated tablets (approval number: national medicine J20130078; Bayer Pharmaceutical and Health Co., Ltd.), 25 mg twice a day (BID);
3. Subcutaneous injection of low-molecular-weight heparin sodium (approval number: Chinese medicine H20010233; Jilin Huakang Pharmaceutical Co., Ltd.), 5000 U once a day (QD)
4. In patients with antiphospholipid syndrome, oral prednisone (approval number: national drug H33021207; Zhejiang Xianli Pharmaceutical Co., Ltd.), 5 to 10 mg QD
5. Oral hydroxychloroquine (approval number: H20160306 (H20140128); manufacturer: Sanofi-Synthelabo Ltd.), 100 to 200 mg BID.

**TCM Treatment**
In addition to the psychological intervention, the BSSG group was treated with the BSSG method with a solution of:

dodder 15 g
*Eucommia ulmoides* 10 g
*Cistanche deserticola* 10 g
antler frost 20 g
cloud *Poria* 15 g
fried *Atractylodes macrocephala* 10 g
patchouli 10 g
*Scutellaria baicalensis* 5 g
tangerine peel 10 g
*Bupleurum* 10 g
raw astragalus 20 g
yam 20 g
*Radix Paeoniae Alba* 10g

**Syndrome additions and deletions:**

1. Dry mouth, or hot flashes and night sweats, red tongue for Yin deficiency syndrome, as appropriate: raw *Rehmannia glutinosa*, *Ligustrum lucidum*, *Polygonatum*
2. Nausea, obesity, white and greasy tongue coating for phlegm-dampness syndrome: white mustard seed and *Pinellia ternate*, as appropriate
3. Common abdominal pain, lesser abdominal pain, anal distension and discomfort, purple tongue or dark pulse astringent syndrome: *Angelica sinensis*, *Angelica sinensis* and *Pinellia ternate*, as appropriate.

**Process.** The herbs are soaked for 30 minutes, boiled with martial fire, then boiled gently for 30 to 45 minutes and 200 to 300 mL of juice is filtered out. Then water is added, the substance is boiled with martial fire, then gently boiled for 10 to 20 minutes and 100 to 200 mL of juice is filtered out, and both juices are combined. The patients were given 200 mL of this solution twice a day: once, warm, in the morning and half an hour after dinner.

The medication was started when the intrauterine pregnancy was diagnosed by color ultrasound. The proportion of the TCM regimen was adjusted according to the change in the patient’s condition up to 14 weeks of pregnancy.

**OUTCOME MEASUREMENT**
TCM syndrome scores, laboratory indices (serum human chorionic gonadotropin [β-HCG], progesterone [P], estradiol [E2], D-D, platelet aggregation rate, Hcy and AT-III) and psychological changes in the 2 groups before and after treatment were calculated and compared. Clinical efficacy, pregnancy outcome and adverse events in the 2 groups after treatment were also noted.

**TCM Syndrome Score**
The score is formulated according to the guiding principles of Clinical Research of New Drugs of traditional Chinese Medicine. The patients were categorized according to the severity of recurrent symptoms: none (0 points), mild (2 points), moderate (4 points) and severe (6 points), and according to the severity of the secondary syndrome: none (0 points), mild (1 points), moderate (2 points) and severe (3 points). The higher the score, the more serious the clinical symptoms.

**Clinical Efficacy**

1. **Cure.** After treatment, vaginal bleeding <5 days, lower abdominal and back pain and other clinical symptoms disappeared; ultrasound examination of uterine size and embryonic development were consistent with gestational weeks
2. Markedly effective. After treatment, vaginal bleeding <7 days, lower abdomen and back pain and other clinical symptoms are significantly improved; ultrasound examination of uterine size and embryonic development were consistent with gestational weeks, and the syndrome integral value was reduced by 70% to 95%

3. Effective. Vaginal bleeding stops within 10 days after treatment, lower abdominal and back pain and other clinical symptoms were improved; ultrasound examination of uterine size and embryonic development were consistent with gestational weeks, and the syndrome integral value was reduced by 30% to 70%

4. Ineffective. Vaginal bleeding more than 10 days after treatment, lower abdominal and back pain and other clinical symptoms were not relieved but aggravated, and the syndrome integral value was reduced by <30%.

Total effective rate = (cure + markedly effective + effective) / total number of cases × 100%

Laboratory indicators

3 to 5 mL of morning fasting elbow venous blood was taken and placed in a dry tube before and after treatment. After 30 minutes of coagulation, 3000 r/min centrifugation (centrifugal radius = 5 cm) was used. After 15 minutes, the serum was separated and stored in the refrigerator at -50°C. Serum β-HCG, P and E2 were detected by Italian VIDAS automatic fluorescence immunoassay; D-D and Hcy were detected by immune turbidimetry kit produced by Roche in Switzerland; AT-III was detected using immune turbidimetry method respectively by ACLTOP700 automatic coagulation analyzer (Instrumentation Laboratory Co., Werfen Company, Bedford, MA USA). Platelet aggregation rate was analyzed and calculated by platelet aggregation analyzer Chro-noLog560Ca.

Mental status. The SAS and SDS scales were used for evaluation. SAS scale: includes a total of 20 items, using a 1 to 4 scoring method. SDS scale: A total of 20 items are included, using a 1 to 4 scoring method. The 20 items on the SAS and SDS scales are divided into rough scores, and the rough scores are multiplied by 1.25 to get standard scores. Among them, the critical value standard of the anxiety evaluation is divided into 50 points; ≥50 points are rated as anxiety, and the higher the score, the more obvious the anxiety tendency. The SDS standard cut-off value is 53 points, and the higher the score, the more severe the patients' depression.

Pregnancy outcome, including clinical pregnancy, persistent pregnancy and early abortion.

Clinical pregnancy: blood or urine β-HCG >25IU/ml or urine pregnancy test positive, and the existence of one or more pregnancy sacs confirmed by ultrasound, including normal intrauterine pregnancy, ectopic pregnancy, intrauterine and intrauterine pregnancy.

Persistent pregnancy: confirmation of pregnancy and lasting pregnancy for more than 12 weeks.

Early abortion: after confirmation of pregnancy, spontaneous abortion (except biochemical pregnancy abortion) within 12 weeks of pregnancy is called early abortion.

Adverse reactions. Symptoms such as rash, nausea and vomiting were carefully noted, and electrocardiogram, liver and kidney function and hematuria routine were examined before and after treatment.

Statistical Analysis

The sample size was estimated using the mean comparison method. \( n = \frac{\left(\mu_{1} + \mu_{2}\right)^{2} + 2/s}{1/2 + \left(1/2\right)^{2}} \), \( n \) was the number of patients in the control group. \( \mu_{1} \) and \( \mu_{2} \) were the percentages corresponding to 1-\( \alpha/2 \) and 1-\( \beta \) in the standard normal distribution. \( t \) was the experimental group mean, \( c \) was the control group mean, \( s \) was the 2-group merged standard deviation and \( k \) was the percentage of patients in the 2 groups. \( \alpha = 0.05 \). \( \beta = 0.01 \),

\[ s = \sqrt{\frac{(n_{1} - 1) s_{1}^{2} + ((n_{2} - 1) s_{2}^{2})}{n_{1} + n_{2} - 2}} \]

\( n_{1} \) and \( n_{2} \) were the number of cases in the 2 groups. \( s_{1} \) and \( s_{2} \) was the standard deviation in the 2 groups. According to the provisions of the China State Food and Drug Administration, 15% was taken as the shedding rate, so the grouped sample size of this study was determined to be \( n = 42 \times 1 / (1-0.15) = 49.41 \approx 50 \).

All the data collected in this study were analyzed using IBM SPSS 23.0 software. Normally distributed measurement data were expressed as mean ± standard deviation (SD) and the comparisons were examined by student \( t \) test. The categorical data were expressed as \( n \) (%), and the differences between the 2 groups were examined by chi-square analysis or Fisher's exact test. \( P < 0.05 \) was considered statistically significant.

RESULTS

Comparison of TCM Syndrome Scores in the Two Groups

Before treatment, there was no significant difference in the scores of primary, secondary or total TCM syndrome between the 2 groups (\( P > 0.05 \)). After treatment, all scores in the 2 groups were lower than before treatment, and scores in the BSSG group were significantly lower than in the control group (\( P < 0.05 \)) (Table 2).

Comparison of Clinical Efficacy in the Two Groups

After treatment, the clinical curative effect in the BSSG group was significantly higher (92% vs 76%) than in the control group (\( P < 0.05 \)) (Table 3).

Comparison of Laboratory Indicators in the Two Groups

Before treatment, there was no significant difference in \( \beta \)-HCG, P, E2, D-D, platelet aggregation rate, Hcy or AT-III between the 2 groups. After treatment, the levels of \( \beta \)-HCG, P, E2 and AT-III in the 2 groups were higher, while the levels...
Table 2. Comparison of TCM Syndrome Scores in the 2 Groups (x ± s)

<table>
<thead>
<tr>
<th>Score</th>
<th>Control Group (n = 50)</th>
<th>BSSG Group (n = 50)</th>
<th>t</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary syndrome score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>38.68 ± 4.21</td>
<td>38.73 ± 4.29</td>
<td>0.059</td>
<td>.953</td>
</tr>
<tr>
<td>After</td>
<td>3.21 ± 0.37</td>
<td>1.02 ± 0.23</td>
<td>-35.545</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Secondary syndrome score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>9.69 ± 1.15</td>
<td>9.76 ± 1.29</td>
<td>0.286</td>
<td>.775</td>
</tr>
<tr>
<td>After</td>
<td>1.21 ± 0.17^</td>
<td>0.65 ± 0.21^</td>
<td>-14.656</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total TCM syndrome score</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>47.37 ± 5.36</td>
<td>48.49 ± 5.58</td>
<td>1.024</td>
<td>&lt;.308</td>
</tr>
<tr>
<td>After</td>
<td>4.42 ± 0.34^</td>
<td>1.67 ± 0.44^</td>
<td>-27.916</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*Compared with the control group before treatment (P < .001)
^Compared with the BSSG group before treatment (P < .001)

**Abbreviations:** TCM, Traditional Chinese Medicine; BSSG, Bushen-Shugan.

Evaluation of D-D, platelet aggregation rate and Hcy were lower than before treatment. Compared with the control group, the levels of β-HCG, P, E2 and AT-III in the BSSG group were increased, but the levels of D-D, platelet aggregation rate and Hcy were decreased and the differences were statistically significant (P < .05) (Table 4).

**Comparison of Mental State in the Two Groups**

Before treatment, there was no significant difference in the SAS and SDS scores in the 2 groups, but the scores were lower in both groups after treatment than before treatment, and the scores in the BSSG group were significantly lower than in the control group (P < .05) (Table 5).

**Comparison of Pregnancy Outcomes in the Two Groups**

There was no significant difference in the clinical pregnancy rate between the 2 groups before treatment, but the persistent pregnancy rate in the BSSG group was higher and the early abortion rate lower compared with the control group after treatment (P < .05) (Table 6).

**Comparison of Adverse Events in the Two Groups**

During treatment, there were 3 cases of skin rash, 4 cases of subcutaneous hematoma and 1 case of gingival bleeding in the control group but no adverse events in the BSSG group. Compared with the control group, the number of adverse events in the BSSG group was significantly lower (χ² = 8.696; P = .006). After treatment, electrocardiogram, liver and kidney function tests, and routine blood and urine tests in both groups were normal.

**DISCUSSION**

Recurrent miscarriage is a common and frequently occurring event in clinical practice, with a 1% to 5% of all pregnancies incidence rate according to relevant studies. The

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Table 3. Comparison of Clinical Efficacy in the 2 Groups

<table>
<thead>
<tr>
<th>Item</th>
<th>Control Group (n = 50)</th>
<th>BSSG Group (n = 50)</th>
<th>χ²</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy classification</td>
<td></td>
<td></td>
<td>4.762</td>
<td>.029</td>
</tr>
<tr>
<td>Cure</td>
<td>12</td>
<td>22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Markedly effective</td>
<td>17</td>
<td>14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effective</td>
<td>9</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ineffective</td>
<td>12</td>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total effective rate n (%)</td>
<td>38 (76%)</td>
<td>46 (92%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** BSSG, Bushen-Shugan.

Table 4. Comparison of Laboratory Indicators in the 2 Groups (x ± s)

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Treatment Time</th>
<th>Control group (n = 50)</th>
<th>BSSG group (n = 50)</th>
<th>t</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-HCG (mIU/ml)</td>
<td>before</td>
<td>20802.93 ± 241.29</td>
<td>20781.82 ± 231.98</td>
<td>-0.443</td>
<td>.659</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>98734.83 ± 621.21^</td>
<td>112876.49 ± 671.98^</td>
<td>109.271</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>P (ng/ml)</td>
<td>before</td>
<td>23.81 ± 4.89</td>
<td>23.87 ± 4.98</td>
<td>0.061</td>
<td>.951</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>31.29 ± 3.48^</td>
<td>37.01 ± 5.23^</td>
<td>6.438</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>E2 (ng/L)</td>
<td>before</td>
<td>484.93 ± 21.24</td>
<td>480.92 ± 23.29</td>
<td>-0.900</td>
<td>.370</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>1523.98 ± 89.93^</td>
<td>2539.49 ± 98.73^</td>
<td>53.769</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>D-D (mg/L)</td>
<td>before</td>
<td>1.61 ± 0.25</td>
<td>1.63 ± 0.28</td>
<td>0.377</td>
<td>.707</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>1.33 ± 0.15^</td>
<td>1.19 ± 0.19^</td>
<td>-4.089</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Platelet aggregation rate (%)</td>
<td>before</td>
<td>67.82 ± 4.92</td>
<td>67.93 ± 5.01</td>
<td>0.111</td>
<td>.912</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>61.29 ± 5.03^</td>
<td>58.92 ± 4.98^</td>
<td>-2.368</td>
<td>.020</td>
</tr>
<tr>
<td>Hcy (µmol/L)</td>
<td>before</td>
<td>11.69 ± 1.31</td>
<td>11.72 ± 1.29</td>
<td>0.115</td>
<td>.909</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>6.93 ± 0.93^</td>
<td>5.39 ± 0.98^</td>
<td>-8.060</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>AT-III(%)</td>
<td>before</td>
<td>42.01 ± 9.01</td>
<td>41.33 ± 8.92</td>
<td>-0.379</td>
<td>.705</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>89.73 ± 9.73^</td>
<td>106.29 ± 12.19^</td>
<td>7.508</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*Compared with the control group before treatment (P < .001)
^Compared with the control group after treatment (P < .001)

**Abbreviations:** β-HCG, human chorionic gonadotropin; AT-III, antithrombin-III; BSSG, Bushen-Shugan; D-D, d-dimer; E2, estradiol; Hcy, homocysteine; P, progesterone.
Table 5. Comparison of the Mental State in the Two Groups (x ± s)

<table>
<thead>
<tr>
<th>Scale</th>
<th>Treatment Time</th>
<th>Control Group (n = 50)</th>
<th>BSSG Group (n = 50)</th>
<th>t</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAS</td>
<td>before</td>
<td>65.87 ± 5.39</td>
<td>65.93 ± 5.49</td>
<td>0.055</td>
<td>.956</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>39.93 ± 4.01</td>
<td>38.82 ± 3.21</td>
<td>-12.541</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SDS</td>
<td>before</td>
<td>66.69 ± 5.49</td>
<td>66.73 ± 5.62</td>
<td>0.036</td>
<td>.971</td>
</tr>
<tr>
<td></td>
<td>after</td>
<td>40.92 ± 3.04</td>
<td>32.82 ± 2.98</td>
<td>-13.522</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*Compared with the control group before treatment (P < .001)

*Compared with the BSSG group before treatment (P < .001)

**Abbreviations:** SAS, Self-rating Anxiety Scale; SDS, Self-rating depression scale.

Table 6. Comparison of Pregnancy Outcomes in the 2 Groups

<table>
<thead>
<tr>
<th>Pregnancy Outcome</th>
<th>Control Group (n = 50)</th>
<th>BSSG Group (n = 50)</th>
<th>x²</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical pregnancy n, (%)</td>
<td>47 (98%)</td>
<td>46 (86%)</td>
<td>0.154</td>
<td>.695</td>
</tr>
<tr>
<td>Persistent pregnancy n, (%)</td>
<td>46 (92%)</td>
<td>38 (76%)</td>
<td>4.762</td>
<td>.029</td>
</tr>
<tr>
<td>Early abortion n, (%)</td>
<td>2 (2%)</td>
<td>8 (14%)</td>
<td>5.983</td>
<td>.014</td>
</tr>
</tbody>
</table>

**Abbreviations:** BSSG: Bushen-Shugan

risk of spontaneous abortion in the next pregnancy of such patients is as high as 70% to 80%, which is a heavy blow to patients’ psychological state. Therefore, partial recurrent abortion will be accompanied by anxiety, depression and other negative psychology. Kolte, et al. confirmed that the incidence of moderate to severe depression in patients with recurrent abortion was 5 times higher than that in women of general childbearing age. A study conducted by He Liying, et al. confirmed that patients with recurrent abortion were more prone to anxiety, depression and other negative psychology than patients without recurrent abortion. These patients can experience serious threats to their physical and mental health, as well as to the life and safety of the fetus if they do not receive timely treatment.

In TCM, there is no name for recurrent abortion combined with anxiety and depression. According to the clinical symptoms of the disease, it is classified as “multiple abortion” and “sliding fetus.” The etiology of this disease is complicated, and the main pathogenesis is the depletion of qi, blood and chong Ren caused by the deficiency of kidney qi, unstable kidney qi and stagnation of liver qi. Therefore, the treatment method is to nourish the blood and the kidneys, calm the heart, calm the nerves, and soothe the liver and regulate qi. The Bushen-Shugan method is based on warming yang and removing turbidity, as taught by professor Xia Tian. The original prescription is mainly for the failure of repeated transplantation of thin endometrium. For tonifying kidneys and soothing the liver, dodder tonifies the kidneys and essence, nourishes the liver and the fetus; Eucommia ulmoides tonifies the liver and kidneys, fixes menstruation and calms the fetus; Cistanche deserticola tonifies kidney yang and nourishing essence blood; deer antler cream warms kidney yang and astringent hemostasis; Yun Poria cocos nourishes the heart and calms the mind; fried Atractylodes macrocephala calms the fetus; patchouli stops vomiting. Scutellaria baicalensis Georgi cools the blood and stops bleeding, removes heat and calms the fetus; tangerine peel regulates qi and middle; Bupleurum soothes the liver, regulates qi and relieves depression; raw astragalus tonifies qi and the surface; Chinese yam strengthens the kidneys and essence; Radix Paeoniae Alba relieves yin and sweat, nourishes the blood and regulates menstruation, and calms the liver yang, softens the liver and relieves pain.

The combined use of various medicines can tonify the kidneys and essence, nourish the liver, fix the fetus, facilitate astringent hemostasis, nourish the heart and mind, soothe the liver, regulate qi and relieve depression. Qian Yanqing, et al. confirmed that a tonifying kidney and soothing liver regimen in patients with recurrent miscarriage complicated by kidney deficiency and liver stagnation can improve the rate of fetal preservation and improve anxiety. The results of our study showed that compared with the control group, the main, secondary and total TCM syndrome in the BSSG group were lower and the clinical effect was higher after treatment, indicating that the BSSG method can effectively treat the clinical symptoms of patients with recurrent abortion complicated by anxiety and depression.

Recurrent miscarriage is associated with insufficient estrogen and progesterone receptors, leading to a decrease in progesterone secretion and decreased P and E2 levels, which affects endometrial development so that it can’t match embryo development speed, affects embryo implantation and development and induces miscarriage. β-HCG is secreted by the trophoblast of the fertilized egg, which can induce the menstrual corpus luteum to become the pregnancy corpus luteum and accelerate the formation of P and E2. The D-D level can effectively reflect secondary fibrinolytic activity in the body; an increase in D-D indicates fibrin thrombosis and fibrinolysis, which is the manifestation of the body’s hypercoagulable state. If the D-D level is high during pregnancy, it will form a thrombus and lead to adverse pregnancy outcomes. Pang Miaomiao, et al. confirmed that patients with recurrent spontaneous abortion had a thrombotic tendency, and the detection of plasma D-D, AT-III, protein C and protein S could predict the possibility of thrombotic events and improve pregnancy outcomes. Tan, et al. confirmed that patients with early recurrent miscarriage had a tendency to develop thrombosis. The detection of D-D combined with AT-III activity can predict the possibility of thrombotic events in recurrent miscarriage and improve pregnancy outcomes. The platelet aggregation rate reflects the index of platelet adhesion characteristics, and is generally approximately 70%. If the platelet aggregation rate is increased, it means that the adhesion between platelets is increased, which is common in the state before thrombosis.

**Abbreviations:** SAS, Self-rating Anxiety Scale; SDS, Self-rating depression scale.

**Table 5. Comparison of the Mental State in the Two Groups (x ± s)**

**Table 6. Comparison of Pregnancy Outcomes in the 2 Groups**

**Abbreviations:** BSSG: Bushen-Shugan
or thrombotic disease, which will cause adverse events in pregnancy.21 Lu, et al.22 confirmed that the platelet aggregation rate was significantly increased in patients with early recurrent miscarriage. The detection of an increased platelet aggregation rate in patients with recurrent spontaneous abortion (RSA) has important clinical diagnostic value. Hcy is an intermediate of methionine metabolites, which is mainly formed by methionine demethylation in vivo, and can be metabolized through remethylation and the sulfur transfer pathway. It is abnormally expressed in patients with recurrent miscarriage.23

A study conducted by Lin, et al.24 confirmed that TCM prescriptions could effectively improve patients’ clinical syndromes, enhance P levels and improve the success rate of fetal preservation. Feng, et al.25 also confirmed that TCM prescriptions could significantly increase the levels of P, E2, β-HCG and other effective indicators in patients with unexplained recurrent miscarriage, and improve pregnancy outcomes. The results of our study showed that compared with the control group, β-HCG, P, E2 and AT-III were all increased, while D-D, platelet aggregation rate and Hcy were all decreased, in the BSSG group after treatment, indicating that the tonifying kidney and soothing liver method can effectively regulate progesterone and blood coagulation function in patients with recurrent miscarriage combined with anxiety and depression.

With the transformation of the medical model from biomedical to bio-social-psychological, psychological factors have received more and more attention in the disease occurrence and development process. Negative psychology such as anxiety and depression affects the neuroendocrine system, which affects the function of various organs in the whole body; it also affects fertilization, implantation, embryo formation and fetal growth, and can even lead to fetal arrest.26 Our study results showed that SAS and SDS scores in the BSSG group were lower than in the control group after treatment, indicating that the BSSG method could effectively improve the psychological state of patients with recurrent miscarriage complicated with anxiety and depression. Wang, et al.27 studied 161 patients with alloimmune recurrent miscarriage, and the results confirmed that the TCM regimen combined with active immunotherapy can reduce the miscarriage rate in patients with alloimmune recurrent abortion and improve pregnancy outcomes. Liu, et al.27 had also confirmed that the TCM prescription combined with low frequency therapeutic apparatus could reduce the probability of recurrent abortion in patients with spontaneous abortion. Li, et al.28 had confirmed that the use of the TCM prescription in the treatment of recurrent miscarriage could result in better pregnancy outcomes. Our study results showed that compared with the control group, the BSSG group had a higher persistent pregnancy rate and a lower early abortion rate after treatment, indicating that the BSSG method could effectively increase the persistent pregnancy rate in patients with recurrent miscarriage with anxiety and depression and reduce the early abortion rate. Our study further analyzed adverse events with use of the BSSG method in the treatment of recurrent miscarriage complicated by anxiety and depression. The results showed that the number of adverse events in the BSSG group was lower than in the control group. After treatment, electrocardiogram, liver and kidney function tests, and routine blood and urine tests in the 2 groups were normal, indicating that the BSSG method had a high safety profile and could also effectively reduce adverse reactions.

CONCLUSION
In conclusion, the Bushen-Shugan method can effectively improve clinical symptoms in patients with recurrent miscarriage complicated by anxiety and depression, regulate levels of serum D-D, platelet aggregation, Hcy and AT-III, progesterone and blood coagulation functions, relieve negative psychology such as anxiety and depression, improve pregnancy state and reduce adverse events. We believe that the Bushen-Shugan method is worthy of clinical promotion and application.

Study Limitations
Our study had some limitations. First, this was a single-center prospective study and the sample size was limited, so the results need to be confirmed by a multicenter study. Second, although randomized patient grouping reduces bias and baseline information was comparable, the inclusion of patients with antiphospholipid syndrome in this study may cause some selective bias that is unavoidable in real-world practice.

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AUTHOR CONTRIBUTIONS
Rong Cang and Zhexia Hu contributed equally to this paper.

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