Clinical Effect of Yunkang Granule Combined with Low Dose Aspirin in the Treatment of Unexplained Recurrent Abortion and Its Influence on Pregnancy Outcome

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Abstract: Purpose: To study the clinical effect of Yunkang Granule combined with low dose aspirin in the treatment of unexplained recurrent abortion (URSA) and its impact on pregnancy outcome. Methods: Seventy-two patients with URSA were randomly divided into a control group and an experimental group. The control group was given conventional treatment, and the experimental group was given pregnancy-kang granules combined with low-dose aspirin. The clinical efficacy of the two treatments and their effects on hormone levels, coagulation function indexes and pregnancy outcome were compared. Results: After medication, the levels of β-HCG, P and E2 in 2 groups were higher than before medication, and the levels of β-HCG, P and E2 in observation group were higher than control group, the difference was statistically significant ($P < 0.05$). Compared with before medication, the levels of coagulation function indexes PT, TT and APTT were increased in both groups after medication, while the levels of FIB were decreased. The levels of coagulation function indexes PT, TT, APTT and FIB in observation group were better than those in control group after medication, and the difference was statistically significant ($P < 0.05$). After treatment, the total effective rate of the experimental group was significantly increased, and the pregnancy outcome was significantly improved. Conclusion: The combination of Yunkang granule and low-dose aspirin in the treatment of URSA has obvious curative effect, can significantly improve the pregnancy outcome, and is worthy of clinical promotion.

Keywords: Yunkang Granule; Aspirin; Recurrent Abortion of Unknown Cause; Clinical Effect; Pregnancy Outcome

Introduction

Recurrent spontaneous abortion (RSA) or recurrent pregnancy loss (RPL) is a recurrent spontaneous abortion (RSA) or recurrent pregnancy loss (RPL) that occurs with the same partner for two or more consecutive or discontinuous pregnancies before 24 weeks[1, 2]. The causes of URSA are complex and varied, including genetic factors, anatomical abnormalities, infection, endocrine abnormalities, immune dysfunction, autoantibody abnormalities (such as antiphospholipid syndrome), thrombotic diseases, etc [3]. However, the etiology of nearly 50% of patients with recurrent abortion is currently unclear, and the clinical diagnosis is URSA or unexplained recurrent pregnancy loss (URPL)[4]. As the etiology and pathogenesis of URSA are still being explored, clinical treatment methods are relatively limited. At present, most therapeutic methods are clinical small sample, observational and experimental studies under the guidance of existing theories, including immunotherapy, anticoagulant therapy, hormone therapy, etc., which still need to be verified by further clinical studies. Yunkang granules are composed of Dixie, Chinese yam, angelica and astragalus, etc., which have the effects of nourishing blood, calming fetus, strengthening spleen and strengthening kidney. Its role in habitual abortion has been verified [5]. This

study intends to discuss the clinical effect of Yunkang granules combined with low-dose aspirin on URSA, and study its influence on pregnancy outcome.

1. Materials and methods

1.1 General data

A total of 72 patients with unexplained recurrent abortion admitted to our hospital from January 2021 to January 2022 were selected as research objects and divided into control group and experimental group according to random number table method, with 36 cases in each group. Patients in the control group ranged in age from 20 to 40 years, with an average age of 30.92±5.88 years. The number of abortions ranged from 2 to 4, with an average of 2.69±0.86. Patients in the experimental group ranged in age from 21 to 39 years old, with an average age of 30.22±5.08 years old; The number of abortions ranged from 2 to 4, with an average of 2.81±0.82. There were no significant differences in age, abortion frequency and other general information between the two groups ($P>0.05$), indicating comparability. This study has been approved by the hospital ethics committee and all patients have signed informed consent.

1.2 Inclusion and exclusion criteria

Inclusion criteria: ①The number of abortion for patients ≧2 times, including biochemical pregnancy is not included, and the gestational week is about 10 weeks； ②Both husband and wife received chromosome examination, chromosome karyotype results showed no abnormal phenomenon, and neither husband and wife had family genetic history； ③Doppler ultrasonography and hysterosalpingography were performed, both of which revealed normal genital anatomy； ④No chlamydia, mycoplasma, treponema pallidum and toxoplasma were infected;⑤The test results of anti-nuclear antibody, anti-phospholipid antibody and anti-sperm antibody were negative.⑥No relevant treatment was received recently and no drugs were taken that affected the observed effect.

Exclusion criteria: ①Patients with hepatic and renal dysfunction and thyroid dysfunction； ②Patients with antiphospholipid syndrome, coagulation dysfunction and organic disease of uterus； ③Laxity of the inner cervix and hereditary disease;④History of venous or arterial embolism； ⑤Who were not willing to participate in the study or had recently taken medications that affected the observation.

1.3 Methods

Control group was given aspirin (Hulunbuir Kangyi Pharmaceutical Co., LTD., National drug approval number H15020766) orally, 75mg/ time, once a day, until 12 weeks of gestation, and then the dose was adjusted according to the patient's situation. Patients in experimental group were administered with oral YunKang granules, 1 bag/time, 3 times/day on the basis of control group. Clinical efficacy was evaluated after 10 weeks of continuous treatment in both groups.

1.4 Obvervational index

1.4.1 Hormone level test

The levels of serum chorionic gonadotropin (β-HCG), progesterone (P) and estradiol (E_2) before and after treatment were observed in two groups.

1.4.2 Detection of coagulation function index

2ml of venous blood was extracted from 2 groups of patients in the morning before and after medication, and serum

was centrifuged at 4℃. Prothrombin time (PT), thrombin time (TT), activated partial thrombin time (APTT) and fibrinogen (FIB) levels were detected by the analyzer, with matching kits and in strict accordance with instructions.

1.4.3 Evaluation of clinical curative effect

The two groups of subjects maintained a pregnancy of more than 28 weeks and successfully delivered a child as a cure, the pregnancy was not successful as invalid.

Total response rate = number of cured cases/total cases.

1.4.4 Pregnancy outcome

Follow-up for 1 year, pregnancy outcome and newborn deformity were recorded in both groups.

1.5 Statistical analysis

SPSS 26.0 software was used to process the data. The measurement data were in line with normal distribution and were expressed as ($\bar{x}$±s). Independent sample T-test was used for comparison between the two groups, and paired T-test was used for differences before and after treatment. The count data were expressed by frequency, and χ^2 test was used to compare the two groups.

2. Results

2.1 Comparison of hormone levels between the two groups

As shown in Table 1, after medication, the levels of β-HCG, P and E2 in 2 groups were higher than before medication, and the levels of β-HCG, P and E2 in observation group were higher than those in control group, with statistical significance (P < 0.05).

Table 1. Comparison of hormone levels between the two groups（ $\bar{x}$±SD）

Indexes	Experimental group（n=36）		Control group（n=36）	
	Prior-treatment	Post-treatment	Prior-treatment	Post-treatment
β-HCG（mIU/mL）	1173.00±81.74	16588.00±1299.00$^{***\#\#\#}$	1156.00±80.59	12325.00±1383.00***
P（ng/mL）	12.85±1.25	36.95±2.63$^{***\#\#\#}$	12.38±1.09	31.63±2.12***
E_2（ng/mL）	271.10±50.26	605.30±51.56$^{***\#\#\#}$	275.30±45.65	547.70±62.42***

Note: *P<0.05，**P<0.01，***P<0.001 VS Prior-treatment；#P<0.05，##P<0.01，###P<0.001 VS control group.

2.2 Comparison of coagulation function indexes between two groups

Compared with before medication, the levels of coagulation function indexes PT, TT and APTT were increased in both groups after medication, while the levels of FIB were decreased. After medication, the levels of coagulation function indexes PT, TT, APTT and FIB in the observation group were better than those in the control group, with statistical significance (P < 0.05, Table 2).

Table 2. Comparison of coagulation function indexes（ $\bar{x}$±SD）

Indexes	Experimental group（n=36）		Control group（n=36）	
	Prior-treatment	Post-treatment	Prior-treatment	Post-treatment

PT（s）	11.24±0.76	14.71±1.16***###	10.91±0.68	12.14±0.96***
TT（s）	12.03±0.60	15.58±0.58***###	12.22±0.45	13.54±0.80***
APTT（s）	24.09±1.55	32.71±1.75***###	24.73±1.30	27.82±1.79***
FIB（g/L）	4.69±0.39	2.80±0.18***###	4.62±0.45	3.64±0.33***

Note: *P<0.05，**P<0.01，***P<0.001 VS Prior-treatment；#P<0.05，##P<0.01，###P<0.001 VS control group.

2.3 Comparison of clinical efficacy between the two groups

After treatment, the total effective rate of the experimental group was significantly higher than that of the control group, and the difference between the two groups was statistically significant (P < 0.05, Table 3).

Table 3. Comparison of clinical efficacy

	Cure	Invalid	Total effective rate（%）
Experimental group（n=36）	33	3	91.67
Control group（n=36）	21	15	58.33
t			3.226
P			0.0019

2.4 Comparison of pregnancy status between two groups

According to statistics, there were statistically significant differences between the experimental group and the control group in the incidence of premature live infants, full-term delivery, abortion/fetal development arrest (P< 0.05, Table 4).

Table 4. Comparison of pregnancy status

	Premature birth living child	term birth	Incidence of miscarriage/fetal arrest
Experimental group（n=36）	2（5.56%）	26（72.22%）	2（5.56%）
Control group（n=36）	6（16.67%）	20（55.56%）	5（13.89%）
t			5.234
P			0.035

3. Discussion

URSA is a special type of spontaneous abortion, with an incidence of about 2% [6], which seriously threatens the physical and mental health, family and social harmony and stability of women of childbearing age. In recent years, URSA has become a hot and difficult topic in the field of reproductive medicine. As the etiology and pathogenesis of URSA are still being explored, the clinical treatment methods are relatively limited, and most empirical therapies, such as traditional Chinese medicine for fetal protection and progesterone therapy, etc. [7], have unsatisfactory therapeutic effects. Therefore, how to improve the therapeutic effect of patients with URSA is still the focus of clinical research.

In this study, 72 patients with URSA admitted to our hospital were randomly divided into two groups, which were respectively given conventional treatment and treatment with Yunkang granules combined with low-dose aspirin. The results showed that after treatment, the hormone level of the experimental group was significantly increased, the coagulation function index was significantly improved, and the total effective rate of clinical treatment reached, and the pregnancy outcome was significantly optimized, which indicated that the combination of pregnancy-kang granules and low-dose aspirin therapy is an effective method for the treatment of URSA, and its mechanism of action needs to be further studied.

In conclusion, the combination of Pregnkang granules and low-dose aspirin in the treatment of URSA has obvious curative effect, indicating the clinical promotion.

References

[1] Bender AR, Christiansen OB, Elson J, et al. ESHRE guideline: recurrent pregnancy loss[J]. 2018; 2018(2): hoy004.

[2] Practice Committee of the American Society for Reproductive Medicine. Definitions of infertility and recurrent pregnancy loss: a committee opinion. Fertil Steril. 2013 Jan;99(1):63.

[3] Ju JG. Clinical effect of didrogesterone combined with low-dose aspirin and low molecular weight heparin in the treatment of unexplained recurrent abortion and its effect on pregnancy outcome [J]. Journal of Clinical Rational Drug Use,2022; 014): 015.

[4] Garrido-Gimenez C, & Alijotas-Reig J. Recurrent miscarriage: causes, evaluation and management[J]. Postgraduate Medical Journal,2015; 91(1073): 151-162.

[5] Yang CR. Clinical study on the treatment of habitual abortion with Pregnancy-Kang Granules combined with choriotropin [J]. Modern Medicine and Clinic, 2019; 9): 3.

[6] Chen JY. Clinical effect of Zishen-yutong Pill combined with dydrogesterone on patients with early threatened abortion complicated with subchorionic hemorrhage [J]. Electronic Journal of Modern Medicine and Health Research,2021; 5(11): 3.

[7] Sun Q, Gao Y, Wang F, et al. Research progress of low molecular weight heparin in the treatment of unexplained recurrent abortion [J]. Hainan Medical Science,2019; 4): 5.

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