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Clinical Study on the Combination of Dingjing Pills and Risperidone in the Treatment of Patients with Schizophrenia Accompanied by Risky Behaviors

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Abstract [**Objectives**] To observe the clinical efficacy of Dingjing Pills on patients with schizophrenia accompanied by risky behaviors. [**Methods**] Two hundred patients diagnosed with schizophrenia and risky behaviors were divided into two groups based on the random and double-blinded principle: the treatment group (100 cases) treated with Dingjing Pills combined with risperidone, and the control group (100 cases) treated with risperidone alone. The observation course was 6 weeks. The clinical efficacy was compared using brief psychiatric rating scale (BPRS), modified overt aggression scale (revised edition) (MAOS), treatment emergent symptom scale (TESS), and blood routine, liver function, kidney function, and electrocardiogram examinations were conducted. [**Results**] After treatment, Dingjing Pills significantly reduced the scores of brief psychiatric rating scale, modified overt aggression scale and treatment emergent symptom scale in patients with schizophrenia and dangerous behaviors, and had no significant toxic or side effects. The total effective rate in the treatment group was 88.8%, while the total effective rate in the control group was 77.1%. There was a significant difference in therapeutic efficacy between the two groups ($P<0.05$). [**Conclusions**] Dingjing Pills has an intervention and therapeutic effect on high-risk behaviors of schizophrenia, with minimal side effects and easy acceptance by patients.

Key words Dingjing Pill, Schizophrenia, Dangerous behavior, Clinical efficacy

1 Introduction

The incidence of aggressive behavior in psychiatric patients is five times higher than that of normal individuals, and 10% of schizophrenia patients have threatening, intense and aggressive behaviors that threaten society and the normal life of families[1]. At present, Western medicines are mainly used for treatment, but their side effects are severe and the compliance is poor, which brings more hidden dangers to patients while treating. Based on the clinical experience of Shiyan Renmin Hospital for nearly 40 years, we developed Dingjing Pills to intervene and treat schizophrenic patients with risky behaviors, showing a positive effect. Now, it is reported as below.

2 Clinical data and methods

2.1 Clinical data Two hundred patients were included in the observation and treatment. All of them were outpatient and inpatient patients in the psychiatric department of Shiyan Renmin Hospital. The diagnosis met following conditions: (i) they met the diagnostic criteria for schizophrenia in the third edition of *Chinese Classification and Diagnostic Criteria of Mental Disorders* (CCMD-3)[2], and changes in hazardous behavior assessed by brief psychiatric rating scale (BPRS)[3] and modified overt aggression scale (revised edition) (MAOS)[4]; (ii) they met the diagnostic criteria of traditional Chinese medicine[5]: according to the diagnostic criteria of the liver fire-entrained phlegm type of schizophrenia in *Practical Traditional Chinese Internal Medicine*; and (iii) patients with suicides, severe physical illnesses, alcohol dependence and drug abuse and pregnant or lactating women were excluded. These patients were randomly divided into two groups according to the order of visits: the treatment group and the control group. There were 100 cases in the treatment group, 65 males and 35 females, aged from 18 to 59 years old, with an average age of (25.30 ± 7.57) years, and the course of the disease ranged from 1.2 to 24.6 years, with an average of 8.76 years. The control group also included 100 cases, 63 males and 37 females, aged from 18 to 55 years old, with an average age of (25.27 ± 7.22) years, and the course of the disease ranged from 1.4 to 23.8 years, with an average of 7.89 years. No significant differences were found in gender, age, and course of disease between the two groups through statistical analysis ($P>0.05$), indicating comparability.

2.2 Methods

2.2.1 Treatment methods. All cases should stop taking medicines for one week before enrollment as a cleaning period.

(i) Control group: Risperidone (trade name Weisitong) was taken alone orally, with an initial dose of 1 mg per day, which was increased to 4 - 6 mg per day within 2 weeks, twice a day. During the treatment period, artane and benzodiazepine drugs should be used as appropriate, and other antipsychotic drugs should not be used. The course of treatment was 8 weeks.

(ii) Treatment group: On the basis of the control group, Dingjing Pills (Bubali Cornu 50 g, Cynanchi Paniculati Radix Et Rhizoma 12 g, Rhei Radix Et Rhizoma 10 g, mirabilite 10 g,

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chlorite schist 30 g, Magnoliae Officmalis Cortex 10 g, Sophorae Flavescentis Radix 15 g, Acori Tatarinowii Rhizoma 20 g, raw oyster shell 30 g, Radix Rhizoma Glycyrrhizae 6 g) was added to make small honeyed pills, which were taken at 10 g each time, 3 times a day, with warm water.

2.2.2 Evaluation methods. All enrolled patients were assessed for changes in their condition using the brief psychiatric rating scale (BPRS) before enrollment and at the end of the 1st, 2nd, 4th and 6th weeks, as well as for changes in their risky behaviors using the modified overt aggression scale (revised edition) (MAOS). The blood and urine routine, liver function, blood biochemistry and electrocardiogram were regularly checked before and after treatment, and evaluation was performed using the treatment emergent symptom scale (TESS).

2.2.3 Efficacy criteria[5]. Before and after treatment, the two groups were evaluated using the BPRS and MAOS (revised version) (Table 1 and Table 2) based on total score reduction rates, with a total score reduction rate >75% indicating significant effectiveness, a score reduction rate in the range of 25% -75% indicating effectiveness, and a score reduction rate <25% indicating ineffectiveness.

2.2.4 Statistical methods. SPSS 19.0 software was used for data processing. The measurement data were compared using ($\bar{x} \pm s$) by t test, and counting data were compared using percentage representation by χ^2 tests. $P<0.05$ indicated a difference with statistical significance.

3 Results and analysis

3.1 Clinical efficacy analysis of two groups As shown in Table 1, after treatment, among the 100 cases in the study group, 2 cases were excluded, 23 cases were clinically cured (23.5%), 39 cases were significantly improved (39.8%), 25 cases were improved (25.5%), and no efficacy was observed in 11 cases (11.2%). Among the 100 cases in the control group, 4 cases were excluded, 18 cases were clinically cured (18.8%), 29 cases were significantly improved (30.2%), 27 cases were improved (28.1%), and ineffective treatment was observed in 22 cases (22.9%). The study group showed a significantly effective rate (recovery + significant improvement) of 63.3%, and an effective rate (significant improvement + improvement) of 88.8%. The values observed in the control group were 49.0% and 77.1%, respectively. There were significant differences in significantly effective rate and effective rate between the two groups ($P<0.05$).

3.2 Comparison of the two groups before and after treatment based on brief psychiatric rating scale (BPRS) and modified overt aggression scale (revised edition) (MAOS) As shown in Table 2 and Table 3, there were no significant differences in the total BPRS score and MAOS score between the two groups before treatment. Since the end of the first week of treatment, the total BPRS scores of both groups and the MAOS score of the study group showed extremely significant decreases compared with before treatment ($P<0.01$). Since the end of the second week of treatment, the MAOS score in the control group exhibited an extremely significant decrease compared with before treatment ($P<0.01$). Compared with the control group, the study group showed more significant decreases in scores of the two scales during the same period ($P<0.05$).

Table 1 Comparison of clinical efficacy between two groups

Group	n	Clinically cured//cases	Significantly improved//cases	Significantly effective rate//%	Improved//cases	Ineffective//cases	Effective rate//%
Study	98	23	39	63.3$^{\triangle}$	25	11	88.8$^{\triangle}$
Control	96	18	29	49.0	24	22	77.1

Note: Compared with the control group, $^{\triangle}P<0.05$.

Table 2 Comparison of BPRS score between the two groups before and after treatment

Group	n	Before treatment	After treatment			
			Week 1	Week 2	Week 4	Week 6
Study	98	57.7 ±9.5	46.4 ±9.0$^{\triangle\#}$	36.1 ±7.7$^{\triangle\#}$	30.4 ±6.1$^{\triangle\#}$	26.3 ±5.2$^{\triangle\#}$
Control	96	58.3 ±10.1	51.1 ±6.5$^{\triangle}$	45.5 ±8.4$^{\triangle}$	35.1 ±6.4$^{\triangle}$	29.2 ±5.1$^{\triangle}$

Note: Compared with the same group before treatment, $^{\triangle}P<0.05$; compared with the control group, $^{\#}P<0.05$.

Table 3 Comparison of MAOS between the two groups before and after treatment

Group	n	Before treatment	After treatment			
			Week 1	Week 2	Week 4	Week 6
Study	98	8.60 ±2.70	8.12 ±2.49$^{\triangle}$	7.21 ±2.45$^{\triangle}$	3.93 ±2.25$^{\triangle\#}$	3.12 ±1.85$^{\triangle\#}$
Control	96	8.86 ±2.87	8.32 ±2.51	7.95 ±2.43$^{\triangle}$	5.76 ±2.33$^{\triangle}$	4.41 ±2.01$^{\triangle}$

Note: Compared with the same group before treatment, $^{\triangle}P<0.05$; compared with the control group, $^{\#}P<0.05$.

3.3 Safety and compliance assessment The side effects of drugs were evaluated using the TESS scale. During the treatment process of the treatment group, there were 2 cases suffering from insomnia and gastrointestinal reactions, 3 cases with extrapyramid-

al symptoms, and 1 case with dry mouth, dizziness, and elevated ALT, and the symptoms were relieved after benzodiazepine drugs, artane, and symptomatic treatment. In the control group, there were 5 cases with extrapyramidal symptoms (EPS), 4 cases with gastrointestinal reaction, 2 cases with dry mouth, dizziness, and elevated ALT, 2 cases with increased heart rate, and 2 cases with irregular menstruation. After receiving benzodiazepine drugs, artane and symptomatic treatment, some symptoms were relieved, and some symptoms were accompanied by treatment. The adverse reactions in the treatment group were significantly less than those in the control group and were easily relieved.

4 Discussion

There have been studies[6] reporting that dangerous or aggressive behaviors that affect patients with mental illness are related to their severe condition and rich mental symptoms. Plain Questions – Great Treatise on the Essentials of Supreme Truth proposes that "all essential fanaticism belongs to fire", and The Classic of Difficult Issues proposes that "those with heavy yin suffer from depressive psychosis, while those with heavy yang have manic-depressive psychosis". Liu Shi believes that the pathological basis for the onset of manic psychosis is the internal blazing of fire evil. Fire indicates the condition of extremely hot, so clearing heat and reducing fire have become the decisive link in treating manic psychosis. If the internal stagnation of fire evil lasts for a long time, it will refine the fluid into phlegm. Phlegm is a tangible yin evil, which is most likely to block the mind. "The heart is the monarch, and the sprit comes out of it", so if the heart monarch is deceived, then the sprit will rebel. Consequently, in the treatment of manic psychosis, the key is to clear phlegm. However, the phlegm of manic psychosis is a pathological product of the internal blazing of fire evil, where tangible yin and intangible evil heat coexist in mutual affection, and it is beyond the ability of ordinary spleen-tonifying and phlegm-resolving drugs. It is necessary to cut off the cause of phlegm generation based on the method of clearing heat. In the formula of Dingjing Pills, Bubali Cornu has the effects of clearing heat, cooling blood, and removing toxic substances, and modern pharmacological studies have shown that it has a significant sedative effect on rats[7]. Cynanchi Paniculati Radix Et Rhizoma has the effects of dispelling wind and dampness, calming the mind and relieving pain, as well as the effect of elevating the qi of the liver and gallbladder to relieve liver stagnation. It has been proven in folk formulas to have therapeutic effects on schizophrenia (crying, sadness, and trance). Sophorae Flavescentis Radix has the effects of clearing away heat and drying dampness. Mirabilite has the effects of purgating heat and bowels, while Rhei Radix Et Rhizoma dissipates heat to remove phlegm and promotes the downward movement of phlegm and fire. When the two drugs are combined, they can enter the Yangming meridian to clean the stagnation of damp-heat in the gastrointestinal tract. Chlorite schist has a heavy weight and is good at treating stubborn phlegm. It has the effects of eliminating phlegm accumulation, calming the liver and relieving convulsion. Acori Tatarinowii Rhizoma has the effect of calming the heart and mind for resuscitation, as well as the effect of dispelling dampness and phlegm. Raw oyster shell is used to suppress yang. Radix Rhizoma Glycyrrhizae has the effect of regulating the middle warmer. The combined use of various herbs achieves the functions of clearing the liver, purging the pathogenic fire, clearing phlegm, and inducing resuscitation.

The results of this study showed that the application of Dingjing Pills combined with risperidone in the study group had a faster and more significant effect compared with the control group using risperidone alone. The aggressive behaviors of most patients disappeared with the relief of mental symptoms, and the combined use of drugs did not exacerbate adverse reactions, so it is worthy of clinical promotion.

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