Clinical Observation on Effect of Xiaoyu Zhixue Tablet (消瘀止血片) on 104 Patients with Idiopathic Multifocal Bleeding and Platelet Aggregation Defect *

Shen Di (沈 迪), Shen Lin (沈 霖), Wang Ailian (王爱莲), Liu Zhongping (刘仲萍)
Yang Rui (杨 锐), Wei Wenning (魏文宁), Yang Yan (杨 焕)
Xiehe Hospital, Tongji Medical University, Wuhan (430022)

ABSTRACT
Objective: To explore the effect and pharmacological mechanism of Xiaoyu Zhixue Tablet (XZT). Methods: XZT mainly composed of Chinese medical herbs to replenish Qi and remove stasis was used to treat patients with idiopathic multifocal bleeding and platelet aggregation defect. Patients were divided into 2 groups, the TCM group (104 cases) treated with XZT, and the control group (84 cases) with vitamin C, K and P, adrenosin and/or artificial menstruation, for at least 4 months. Results: The hemostatic effective rate was 92.3% in the TCM group and 27.4% in the control group (P < 0.005), the recovery rate of platelet aggregation after 6 months’ therapy was 69.2% and only 1.8% respectively. The difference between the two groups was very significant (P < 0.005). Conclusion: XZT could regulate the hemostatic action and platelet aggregation.

KEY WORDS: multifocal bleeding, platelet aggregation defect, Xiaoyu Zhixue Tablet

Clinical curative effect of self formulated Xiaoyu Zhixue Tablet (XZT, a time-honored preparation of Chinese herbal medicine) on 104 patients with idiopathic multifocal bleeding and platelet aggregation defect (IMBPAD) was observed in the recent 3 years by the authors, the effect was satisfactory.

METHODS
Clinical Materials
All the patients were outpatients of the specific clinic of the authors’ hospital. The 104 patients in the TCM group were 31 men and 73 women, with their age ranging from 9 to 62 years, 32.6 years in average. Their main clinical manifestation was multifocal bleeding, including ecchymosis or petechia of limbs in 76 cases, menorrhagia in 34 ( > 100 ml in each cycle), gum bleeding in 36, epistaxis in 32, fundus hemorrhage in 4, and conjunctival bleeding in 2. Their blood pressure and heart rate were normal, their tongue pale in color with petechia, coated with thin fur, pulse taut and uneven. All of them were examined by specialists of internal medicine, otolaryngology, gynecology, stomatology and ophthalmology, yet with no special pathologic lesion found. The 84 patients in the control group were 20 men and 64 women, with their age ranging from 10 to 58 years, 28.5 years in average, course of disease 1 - 11 years. Their hemorrhagic position was ecchymosis or petechia of limbs in 50 cases, menorrhagia in 25, gum bleeding in 27 and epistaxis in 19. The difference in age, course of disease and condition of bleeding between the two groups was insignificant, P > 0.05.

Laboratory Examination
Laboratory tests including blood platelet count, bleeding time, coagulation profiles (activated partial thromboplastin time, prothrombin time and thrombin time were all included) of all patients, and plasma fibrinogen and platelet membrane glycoprotein IIb - IIIa of part of the patients, were examined and no abnormal finding was observed.

Platelet aggregation tests were performed by Chronolog 430 model aggregometer with aggregation inducing agents of adenosine...
diphosphate (ADP, with final concentration of 1.90 μmol/L), arachidonic acid (AA, final concentration 0.37 mmol/L) and platelet activating factor (PAF, final concentration 150 nmol/L). All the three reagents were products of Sigma Co. Routine procedure was adopted to test the maximum aggregation rate (MAR). The result was considered as aggregation response defect when MAR level was within 21% - 40%, and as aggregation response absence when MAR was below 20%(1). Patients with low aggregation response was diagnosed as IMBPAD.

In the TCM group, there were 7 patients who failed to respond to the single agent ADP, 16 to AA and 10 to PAF; 8 failed to respond to 2 agents ADP-AA, 7 to ADP-PAF and 25 to AA-PAF. Thirty one cases failed to respond to all the three, and all were checked by Ristocetin test to rule out hereditary thrombasthenia. The condition of platelet aggregation defect in the control group was 5 failed to respond to ADP, 12 to AA, 8 to PAF, 6 to ADP-AA, 7 to ADP-PAF, 20 to AA-PAF and 26 to all three. The difference between the two groups was insignificant, P >0.05.

Treatment

XZT was mainly composed of Radix Astragalus, Radix Codonopsis Pilosula, Radix Paeoniae lactiflora Alba, Radix Angelica Sinensis, Semen Persica and Radix Glycyrrhiza in ratio of 1.0:1.0:1.0:0.5:0.5:0.2. It was prepared by Wuhan Pharmaceutical Factory with the herbal drugs purchased from Hubei Provincial Company of Chinese Medicinal Materials, and processed into tablets, each containing 1.2 g of crude drugs.

According to the condition of patients, 5 - 8 tablets were given twice a day, or three times a day to patients with severe bleeding such as epistaxis or menorrhagia. Other Chinese and western medicine were all discontinued in the XZT treatment period except vitamin C (100 mg twice a day) and vitamin B complex (1 g, twice a day).

The control group was given vitamin C 100 mg, vitamin K₄ 2 mg, vitamin P 20 mg and adrenobazon 2.5 - 5 mg orally twice a day. Among them, 12 patients of menorrhagia had taken artificial menstruation, besides, 3 male and one female patients of epistaxis had taken prednison 10 mg three times a day for 2 - 3 weeks.

The therapeutic course for both groups was over 4 months.

Indexes of Observation

The platelet count, blood coagulation profiles, platelet aggregation rate and bleeding symptoms were re-examined every 2 months. As the curative effect of conventional treatment was unsatisfactory, the 61 patients in the control group changed to receive TCM treatment, after 4 - 6 months’ observation.

Statistical Analysis

Therapeutic effects of the two groups were compared with χ² test for correlation analysis of enumeration data.

RESULTS

Standard for Effectiveness Evaluation

Since the standard for IMBPAD was lacking at present, the self-set standard, which was established according to clinical practice and repeated laboratory examinations on platelet count and coagulation profiles, was used in the study. The standard included two parts, the standard for hemostatic effect and the standard for platelet aggregation recovery effect.

The standard for hemostatic effect was: (1) Markedly effective: Bleeding was stopped, amount of menstruation normalized (<80 ml per cycle) after 2 months of treatment; (2) Effective: Bleeding stopped, but petechia or gum bleeding occurred accidentally in 2 months after ending treatment. (3) Ineffective: Bleeding still recurred after 6 months treatment or failed to get improved, or even worse.