CLINICAL EXPERIENCE

Clinical Study of Pai-Neng-Da Capsule (派能达胶囊) in the Treatment of Chronic Aplastic Anemia*  

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ABSTRACT  Objective: To evaluate the efficacy and safety of Pai-Neng-Da Capsule (派能达胶囊, panaxadiol saponins component, PND), a new Chinese patent medicine, on patients with chronic aplastic anemia (CAA) and to explore the optimal therapeutic regimen for CAA. Method: A total of 36 patients with CAA were enrolled and divided into three groups: the AP group (20 cases, andriol 120 mg/day + PND 240 mg/day), the ACP group (13 cases, andriol 120 mg/day + cyclosporine 3–6 mg·kg⁻¹·day⁻¹ + PND 240 mg/day), and the PND group (3 cases, PND 240 mg/day). All patients were treated and followed up for 6 months. Peripheral blood counts, renal and hepatic function and Chinese medical (CM) symptoms of patients were assessed and all indices were gathered at the beginning and end of the study. Result: In the AP group, no significant hematologic difference was observed at the end of 6-month treatment comparing with the beginning. In the ACP group, the blood counts were maintained at the same level after the 6-month treatment. In the PND group, trilineage hematologic improvement was displayed at the end of 6-month treatment comparing with the beginning. No significant difference was showed in renal and hepatic function in all patients. All patients' clinical symptom improved according to CM symptom score. The effective rates were 95%, 73% and 100%, respectively. Conclusion: PND improved the efficacy and decreased side effects by cutting down the dosage of andriol, and it could also improve patients' clinical symptom and quality of life. PND were effective and safe in the treatment of CAA, it could be used alone or in combination with pharmacological agents such as andriol and cyclosporine.  

KEYWORDS  chronic aplastic anemia, new Chinese Patent medicine, panaxadiol saponins component

Chronic aplastic anemia (CAA) is a kind of refractory hematological diseases, the major clinical manifestations were anemia and often accompanied by infection and bleeding. In China the incidence of aplastic anemia is 7.4/10⁵ and CAA accounts for 4/5 of them. At present, CAA is routinely treated by androgen, immunosuppressive agents, blood transfusion and Chinese medicine (CM). However, the efficacy of these treatments is variable and uncertain. In addition, they frequently cause serious side effects. There is a need to search and develop new Chinese patent medicines that are more effective and safer. The biological active component in ginseng extract, panaxadiol saponins component, was isolated from total saponins of ginsenosides by application biological activity assays of hematopoiesis, and formulated into capsules named as Pai-Neng-Da (派能达, panaxadiol saponins component, PND), which is a class-five new Chinese patent medicine. The composition and content of PND have been analyzed and defined as five monomers of panaxadiol saponins. The patent of PND for treating variety of pancytopenia has been authorized by the State Intellectual Property Office of China. PND was used subsequently for a series of pharmacodynamics studies, toxicological studies as well as clinical studies. All research data of 23 items were submitted to China Food and Drug Administration (CFDA), and two certificates of new class-five Chinese patent medicine were authorized and granted by CFDA in 2010, including both PND Capsule (approval No. 2010L00856) and panaxadiol saponins component (approval No. 2010L00857),...
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then successfully transferred to Ningbo Tianzhen Pharmaceutical Co. Ltd. for clinical trials and commercial production. PND was demonstrated to be safe, and 6–10 tablets daily were recommended as safe dose in phase I clinical trial. Phase II clinical trial was carried out in seven hospitals with professional advantage for treating primary immune thrombocytopenic purpura (ITP) and chronic agnogenic leukocytopenia (neutropenia). The clinical results confirmed that PND was effective without adverse side effect. Based on previous studies, as supported project, this study used PND alone or in combination with reduced andriol and cyclosporine to observe the efficacy and safety of PND in the treatment of CAA, and to explore the optimal therapeutic regimen for CAA.

METHODS

Inclusion and Exclusion Criteria

The CAA patients were diagnosed according to "Standard for diagnosis and therapeutic efficacy evaluation of hematopathy (3rd edition)". As other forms of pancytopenia diseases such as myelodysplastic syndrome were ruled out, patients who failed to receive routine anti-anemia treatment and volunteered to participate the study were included. Written informed consents were obtained from all patients prior to study participation.

Exclusion criteria included: pregnant or ready for pregnancy women, breastfeeding women; patients with severe cardiovascular, hepatic, renal system or mental disease; patients complicated with severe infection; patients suffered from untreated other hemorrhagic disease or other malignant diseases at the same time.

CM Diagnosis Standard of CAA

According to "Guiding Principle of Clinical Research on New Drugs of Traditional Chinese Medicine", diagnosis was made based on the presence of 2 main CM symptoms and at least 3 secondary CM symptoms plus specific tongue and/or pulse properties in CM diagnosis. The main symptoms included dizziness, fatigue, pale lips and nails, cold limbs, night sweats, hot palms and soles, pale tongue with white coating or thin delicated red tongue with dry coating, thin weak pulse or rapid pulse. The secondary symptoms included palpitation, fever, dry mouth and thirsty, hemorrhage, soreness and weakness of waist and knees, dry stool, sexual dysfunction, abdominal distension, dry stool or pond, impotence, spermatorrhea.

Drugs

PND Capsule was provided by Zhejiang Provincial Hospital of Traditional Chinese Medicine and Ningbo Tianzhen Pharmaceutical Co. Ltd., China (batch No. 20120101). Specification: size 4 gelatin capsules, 40 mg per capsule, each capsule contained five panaxadiol saponins monomers with a purity of 92.44% as analyzed and defined by high-performance liquid chromatography (HPLC) using specific monomers of ginsenosides as the reference standards.

Study Design

A total of 41 patients with a diagnosis of CAA were included in the study at Jinhua People's Hospital between February 2012 and October 2013. The patients were divided into three groups according to patients' disease course and treatment history. Twenty-two patients in the AP group were orally administered with andriol + PND, 15 patients in the ACP group received andriol + cyclosporine + PND, and 4 patients in the PND group were treated with PND alone. PND was administered orally at a dose of 240 mg/day, cyclosporine was given 3–6 mg/(kg·day), and andriol was reduced from 160 to 120 mg/day. All patients were scheduled for 2 treatment courses over 6 months. Blood count, hepatic function, renal function and CM symptoms of patients were assessed at study entry and the end of treatment. This study was approved by Science and Technology Bureau in Jinhua City as a research project for clinical study, and was approved by the Ethics Committee of Jinhua People's Hospital.

Efficacy Evaluation

Western Medical Standards

Therapeutic efficacy was evaluated according to "Standard for diagnosis and therapeutic efficacy evaluation of hematopathy (3rd edition)", which was categorized into four grades. (1) Basically cured: hemoglobin (Hb) increased to 120 g/L in males and 100 g/L in females, white blood counts (WBC) raised to \(4 \times 10^9/L\) and platelet (Plt) counts elevated to \(80 \times 10^9/L\); no symptoms of bleeding and anemia; no recurrence during a follow-up period of 1 year. (2) Remission: no symptoms of bleeding and anemia; Hb recovered to 120 g/L in males and 100 g/L in females, WBC elevated to \(3.5 \times 10^9/L\), Plt was somewhat raised, and all sustained for over 3 months. (3) Markedly improved: symptom of bleeding and anemia improved