Current Treatment Status of Renal Anemia & New Drug Research and Development Situation of our Institute

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Abstract
Renal anemia results from not only relative or absolute insufficiency of erythropoietin (EPO) caused by different kinds of kidney diseases, but also some toxic substances in uremia patients’ plasma which are interfered with production and metabolism of RBC [1]. It is one of the major complications of chronic renal failure (CRF). Its extent is positively correlated with renal hypofunction degree. Renal anemia can occur when chronic glomerular filtration function decreases by more than 50 percent. Renal anemia has high incidence in crowd with chronic kidney disease (CKD). Its effective treatment has a great influence on CRF patients’ prognosis and their life quality. If renal anemia is untreated or improper treated, it may cause many kinds of physiological abnormalities, including oxygen transport and reduction in tissue oxygen utilization, increase of cardiac output, cardiac enlargement, ventricular hypertrophy, angina, heart failure, decline of cognitive ability, allergy, menstrual disorder, sexual dysfunction, and decline of immune function and so on. Therefore, correction of renal anemia posses an important clinical significance.

INTRODUCTION
Current treatment status of western medicine
The treatment of renal anemia is now mostly adopting comprehensive treating measures, including recombinant human EPO treatment, maintenance chronic dialysis, kidney transplantation, adequate nutrient intake, a little blood transfusion, prevention and correction of metabolic acidosis and electrolyte imbalance, prevention of infection, treatment of bleeding tendency and so on [2]. Long-term medical treatment includes complementing chalybeate and folic acid. At present, the clinical efficacy of EPO in correction of renal anemia has been proved by plenty results of clinical and animal experiments. As for the patients whose serum creatinine is equal or greater than 176.8 umol/L, the most likely causation of anemia is lack of EPO [3]. Therefore, the application of EPO is an important part in treatment of CKD patients’ anemia.

Chinese medicine for understanding renal anemia
Renal anemia belongs to Chinese medicine disease categories of Xulao, dizziness, lumbago, kidney overstrain and so on. The location of this disease is kidney, and its main pathogenesis are nephron loss, weakness of the spleen and stomach, embodied domination of pathogen, weakness of the five internal organs, deficiency of qi and blood caused by consumptive disease. The occurrence of this disease is always associated with kidney, spleen, stomach. Kidney stores essence and the main bone produces marrow. The kidney’s function of producing marrow contains marrow hematopoietic system which is recognized by modern medicine. The spleen governs the blood and the kidney stores essence. Essence and blood share with the same origin. Essence and blood interact each other, which is mainly correlated to kidney and spleen. As a result, diagnosis and treatment are mostly adopting the therapies of invigorating spleen and kidney, tonifying kidney and qi, reinforcing deficiency and clearing turbidity, etc.

Chinese medicine research and development situation of our institute
Ginseng has the effect of reinforcing qi and nourishing blood and its mainly effective components is total ginsenoside extracted from Ginseng Root, which was studied in our hospital since 1993. We have proved that total ginsenoside can not only promote the proliferation of hematopoietic stem/progenitor cells, but also induce them to differentiate towards erythroid cells and myeloid cells. Meanwhile, we developed the total ginsenoside ginseng as...
our hospital's drug, named as Shengxueling Capsule, which was the first-generation product. It has been applied in the treatment of patients with different kinds of hemocytopenia [4].

The second-generation product of Pai-neng-da (PND) capsules, containing effective component of Panaxadiol, isolated from total ginsenoside. It has successfully obtained two certificates awarded by Food and Drug Administration of China (CFDA) as new Chinese patent medicine for clinical trial permission [5]. We have proved that component of Panaxadiol possess dual effect of promoting hematopoiesis and regulating immune function in pancytopenia caused by renal anemia [6,7].

(1) PND and Pai-neng-da (PND) capsules has obtained two certificates as new Chinese patent medicine for clinical study. They are transferred to the pharmaceutical enterprise as a technology secret. Now period I clinical trial has been completed, and the safety of the new medicine has been proved.
(2) The unblinding result of PND capsules treating ITP IIa period clinical trial suggests definite efficacy. And there are no obvious side effects. After two-month treatment with 6 PND capsules (240mg) per day, markedly effective and moderate effective cases account for 37.6%, while in placebo group is 0%. (ITP therapeutic effect criterions are classified into markedly effect, moderate effect, improvement and failure. Center for Drug Evaluation (CDE) of Food and Drug Administration of China (CFDA) regards markedly effective and moderate effective cases as effective cases.) After the treatment, the average platelet count of the patients in PND treatment group has risen by $9.97 \times 10^9/L$, while in placebo group has fallen by $3.60 \times 10^9/L$. The therapeutic effect shows significant difference in those two groups.

After two-month treatment with 6 PND capsules (240mg) per day, the platelet count of patients in treatment group increases apparently, while in placebo group decreases.

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(3) As a key funding program (2011ZDA021) of provincial
medical and health platform, in this clinical research, 41 patients are treated only with 6 PND capsules (240mg) per day for three months. It turns out that markedly effective and moderate effective cases account for 39.0% (4 markedly effective cases, 12 moderate effective cases, 7 improved cases, 18 ineffective cases). The average platelet count has risen by 23.02 ± 37.28×10⁹/L, which completely accords with clinical research results of the period IIa.

Treating 41 patients only with 6 PND capsules (240mg) per day for three months, the platelet count of the patients in treatment group is obviously higher than before treatment. The average platelet count has risen by 23.02 ± 37.28×10⁹/L.

In the treatment, 41 patients are treated only with 6 PND capsules (240mg) per day for three months. It turns out that markedly effective and moderate effective cases account for 39.0%, which completely accords with clinical research results of the period IIa (the outcome of the report is earlier than unblinding time of the period IIa).

(5) Establish mice model and rats model to observe the therapeutic effect of PND capsules. After PND treatment, the platelet count increased significantly. And PND treatment can reduce the compensatory increase in the number of bone marrow megakaryoblasts and promegakaryocytes, which promotes them maturing into thrombocytogenic megakaryocytes. PND participates in immune regulation process through inhibiting phagocytosis frequency and index of peritoneal macrophages. By means of PND treatment, CD4+ and CD25+ cell population are increased, and CD4+ /CD8+ cell ratio rises, thus make abnormal T lymphocyte subsets basically return to normal.

CONCLUSION

Summarizing modern medicine’s research to renal anemia, it is discovered that EPO is the main hormone to promote the formation of RBCs and increase hemoglobin. When the kidney is widely damaged, the production of EPO will decrease [8,9]. The spleen has certain hematopoietic function. When the bone marrow function is damaged, spleen can make compensatory extramedullary hematopoiesis. Meanwhile, the combined treatment can also reduce the dosage of EPO, it can partly substitute the kidney function of producing EPO, and another advantage of EPO can prolong dialysis patients’ survival time and improve their living quality. Modern therapy in combination with Chinese Medicine can improve the efficacy and reduce the dosage of EPO in the treatment of renal anemia.

REFERENCES