

**Cyclophosphamide in the Treatment of
Panniculitis Associated Acquired Lipodystrophy
Syndrome With Type 1 Diabetes
2019-04-09**

Informed consent form

Dear parents of _____:

Your child is diagnosed with panniculitis associated acquired lipodystrophy syndrome in our hospital with type 1 diabetes. The panniculitis associated acquired lipodystrophy syndrome is a rare metabolic disease caused by autoimmune reaction that can cause severe insulin resistance. Type 1 diabetes is a metabolic disease in which insulin is absolutely deficient due to autoimmune reactions and requires insulin injection therapy. At present, there is no treatment for panniculitis associated acquired lipodystrophy syndrome in China. The comorbidity of the two diseases leads to a much larger dose of insulin than the other children, but it is still difficult to effectively control blood glucose. As the disease progresses, poor long-term glycemic control can lead to early diabetes-related complications, damage children's health and even death.

Cyclophosphamide is a classic immunosuppressive agent widely used in the treatment of children with autoimmune diseases. However, the application of cyclophosphamide to panniculitis associated acquired lipodystrophy syndrome with type 1 diabetes is a new treatment.

Before you decide whether to take part in the treatment, please read the following as carefully as possible. It can help you understand the treatment and why to take the

treatment, and the benefits, risks and discomforts that may be brought to you by taking part in the treatment. If you want, you can also discuss it with your relatives and friends, or ask your doctor for explanation and help you make a decision.

1. Background, purpose and significance of new technology

Panniculitis associated acquired lipodystrophy syndrome is a rare type of metabolic disease with unknown etiology. Studies suggest that its pathogenesis may be related to autoimmune response. In patients with panniculitis associated acquired lipodystrophy syndrome, the extreme lack of subcutaneous fat, leptin deficiency and fat deposition in the liver and muscles lead to hyperinsulinemia, insulin resistance, and a very high risk of diabetes, hypertriglyceridemia and fatty liver.

Type 1 diabetes is a major disease that threatens human health. Chronic complications of diabetes restrict the long-term survival of diabetic patients. Studies have shown that 20% to 40% of patients will develop diabetic nephropathy; in 5-10 years of illness, about 58% ~80% of people with diabetes develop diabetic eye disease; and after 20 years of illness, 99% of diabetic patients develop diabetic eye disease. Even in children and adolescents with an average disease duration of only 4.9 years, the incidence of diabetic eye disease is as high as 36%.

Patients with acquired lipodystrophy syndrome and type 1 diabetes both have severe insulin resistance and absolute insulin deficiency, so they need to rely on several times dose of insulin than other common type 1 diabetes patients to control blood sugar, but still often cannot get satisfactory results. This may increase the risk of chronic

complications of diabetes, bring complications forward, and seriously affect the health of patients.

Cyclophosphamide is a commonly used immunosuppressive agent in patients with autoimmune diseases. It is mature in usage and controllable in adverse reactions. It is one of the first choices for autoimmune diseases such as childhood nephrotic syndrome, systemic lupus erythematosus and rheumatoid arthritis. It can also be used in patients with autoimmune disease-associated panniculitis who cannot use glucocorticoids. Given that autoimmune factors may be the common cause of panniculitis associated acquired lipodystrophy syndrome and type 1 diabetes, cyclophosphamide may improve the insulin resistance of these patients from the etiology and reduce the amount of insulin; preventing disease progression and even lead to clinical cure.

2. Interventions and advantages

The new technology will be carried out as follows: (1) confirmed by fat biopsy, genetic analysis and clinical analysis, and finally diagnosed as panniculitis associated acquired lipodystrophy syndrome; (2) identified as Type 1 diabetes based on islet function and islet-associated autoantibodies; (3) admission to the hospital to assess the condition, exclusion of cyclophosphamide application contraindications; (4) monthly admission for cyclophosphamide treatment and comprehensive assessment, a total of 6 months; (5) after the end of cyclophosphamide treatment, enter the outpatient follow-up phase. Cyclophosphamide is an immunosuppressive agent that has been widely used in children with autoimmune diseases for a long time. Clinically, it has accumulated rich

experience in the use and dosage of cyclophosphamide, indications and contraindications, and prevention and control of adverse reactions.

3. The current diagnosis of the child and the possible benefits this new technology may bring to the child

Your child is eligible for a diagnosis of panniculitis associated acquired lipodystrophy syndrome. This treatment can regulate the patient's immune system, inhibit the occurrence of autoimmune reactions, delay and improve panniculitis and fat malnutrition, thereby correcting insulin resistance. If the treatment is effective, the blood glucose control of the child will be improved, and the use of insulin and hypoglycemic drugs can be reduced, the chronic complications caused by diabetes and hyperglycemia can be alleviated, and the goal of improving health and quality of life can be achieved.

4. Possible adverse reactions, risks and risk prevention measures

Cyclophosphamide as an immunosuppressive agent may cause the following adverse events, but the following adverse events may not be entirely caused by the drug, and may be related to the disease itself or other causes:

1. Infection: There may be infections of various organs, including bacteria, fungi, viruses and other pathogens, especially lung infections and intracranial infections, which can be life-threatening in severe cases.

2. Important organ damage: There may be damage to important organs, such as heart,

liver, kidney, lungs, etc. Some damage may not be fully restored even if the drug is stopped.

3. Myelosuppression: anemia which is difficult to correct; thrombocytopenia, bleeding such as mucous membrane bleeding, digestive tract, urinary tract bleeding, intracranial hemorrhage and other parts of the bleeding; granulocyte reduction, various serious infections, septicemia, shock, etc.

4. Musculoskeletal and nervous system damage: cause muscle weakness, numbness of the limbs, headache, blurred vision, etc; may induce epilepsy. Osteoporosis can cause femoral head necrosis and fracture deformation in severe cases.

5. Gastrointestinal reactions.

6. Phlebitis.

7. Reproductive system toxicity.

8. Drug allergies, anaphylactic shock, etc.

9. Other unforeseen, unpredictable and precautionary situations: Long-term use increases the risk of developing a tumor.

10. There are other unpredictable risks and adverse reactions and consequences that may jeopardize the life of the child.

In the course of treatment, the doctor will observe your child's condition at any time. If there is any discomfort in the process of diagnosis and treatment, please contact the doctor who is in charge. The doctor will treat any discomfort and adverse reactions in time. Throughout the treatment process, risk prevention measures will be strictly implemented, including eliminating contraindications, strictly following the treatment

process and norms, and closely monitoring the vital signs and indicators of the subjects.

5. Alternatives

If you decide not to take part in this new technology treatment program, we will continue to provide your child with traditional treatments for insulin injection combined with oral hypoglycemic agents.

6. Relevant expenses

The cost of participating in this treatment is entirely at the patient's own expense, and can't be reimbursed through the Children's Fund. The patient will consult with the insurance company on his own whether other commercial insurance can be reimbursed or not.

7. Is personal information confidential?

Your child's medical records (including medical records, physical and chemical examination reports, etc.) will be kept intact in the hospital. Doctors, professional academic committees, ethics committees and health supervision and management departments will be allowed to access your medical records. The public report on the results of this new technology will not disclose your child's personal identity. We will make every effort to protect the privacy of your child's personal medical data within the limits permitted by law.

8. How to get more information?

You can ask any questions about this treatment at any time. Your doctor will leave you a call so that you can answer your questions.

9. Voluntary participation in treatment and withdrawal from treatment

Whether you take part in treatment depends entirely on your willingness. You may refuse to participate in the treatment or withdraw from the treatment at any time during the treatment. Your doctor or therapist may suspend your participation at any time for your best interests. If you do not participate in this treatment, you may withdraw halfway. If you choose to take part in this treatment, we hope you can persist in completing the whole treatment process.

10. What should do now?

Whether to participate in this treatment, you can discuss with your family, children, relatives before making a decision. Before you make a decision to participate in the treatment, please ask your doctor as many questions as possible until you fully understand the treatment.

To ensure your accurate understanding of the above, read the informed consent carefully and make a decision.