Clinical study protocol
Programme No.: ajsfmtxy001

The effect of amino acid peritoneal dialysis fluid on the nutritional status of patients with maintenance peritoneal dialysis was investigated

Efficacy and safety: a multicenter, open, prospective, self-controlled clinical trial research

Peritoneal dialysis Center, Gaozhou People's Hospital

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scenario summary

title	To explore the effectiveness of amino acid peritoneal dialysis fluid in improving the nutritional status of patients undergoing maintenance peritoneal dialysis and safety: a multicenter, open, prospective, self-controlled clinical study
Applicant	Peritoneal dialysis Center, Gaozhou People's Hospital
purpose of research	To explore the effectiveness and safety of amino acid peritoneal dialysis fluid on the nutritional status of peritoneal dialysis patients performance assessment
research design	Multicenter, open, prospective, self-controlled study
Study duration	Each subject will be studied for six months, and the entire study will be completed in about a year.
Number of researchers	140 patients with malnutrition were selected for peritoneal dialysis
Center number	Five centres are expected
Main research unit	Peritoneal dialysis Center, Gaozhou People's Hospital
Criteria for inclusion	1. Patients with malnutrition in uremia were screened and maintained peritoneal dialysis for at least 3 months. The criteria for malnutrition should meet at least 2 of the following items:(1) serum albumin level <3.5g/dL (35g/L), (2) prealbumin <300mg/L, (3) modified Good Law Subjective Comprehensive Nutritional Assessment (Subjective Global Assessment, SGA)> 7 points; 2. Blood urea nitrogen less than or equal to 38mmol/L; 3. The patient's age is between 18 and 75; 4. The patient signs the informed consent form.

Exclusion criteria	1. Allergy to any amino acid or excipient in this product; 2. Have had peritonitis more than once in the last 3 months; have had peritonitis in the last 1 month inflammation or hospitalization; 3. Combine hyperthyroidism, systemic infection fever and other high metabolic state diseases, as well as taking medication drugs that affect tissue metabolism, such as corticosteroids; 4. Congenital amino acid metabolic defects, acute severe pancreatitis, severe hyperbilirubinemia 5. Malignant tumor metastasis or diffusion, residual cancer after treatment, coagulation dysfunction, regeneration patients with obstructive anemia, severe diseases of other systems such as heart, brain and lung; 6. Kidney transplant may be accepted during the trial; 7. Active hepatitis B or C, cirrhosis, active liver disease, liver dysfunction or human immunodeficiency virus (HIV) serum reaction positive; 8. Participants who have participated in other drug clinical trials within 3 months before enrollment; 9. Pregnant and lactating women; 10. The mental state cannot cooperate; 11. No written informed consent has been signed; 12. Unable or unwilling to comply with the protocol approved by the investigator;

The patient withdrew	Participants can withdraw from the study under any circumstances and should do so in the following situations withdrawal studies: (1) The patient develops life-threatening complications; (2) The occurrence of intolerable clinical symptoms related to the therapeutic drug; (3) Pregnancy was combined during the study; (4) Violation of the test plan; (5) Unwilling to continue participation in the study; (6) Disappearance.
Study treatment	Each subject received a daily dose of 1 bag of amino acids for 6 months plus 2-4 daily treatment with bagged glucose peritoneal dialysis fluid.
Research process	Each subject received a 6-month treatment of 1 bag of amino acid peritoneal dialysis and 2-4 bags of glucose peritoneal dialysis fluid per day (the amount of glucose peritoneal dialysis fluid was determined according to the treatment protocol at screening when the patient entered the study). Before and during treatment, in the 1st, 3rd and 6th months, the subjects were evaluated for various efficacy and safety indicators Estimate and record any adverse events or serious adverse events. Follow up monthly during treatment assess subjective feelings (infusion pain, abdominal distension), blood pressure, weight, urine volume, and ultrafiltration.

Endpoint of efficacy	Efficacy indicators: serum albumin, prealbumin and body mass, body mass index (Body mass index, BMI), lean body mass index (con icity index, CI), waist circumference and grip strength, upper arm muscle circumference, standardized protein catabolic rate (Normalized protein catabolic rate, nPCR), standardized protein total nitrogen excretion rate (Normalized protein nitrogen appearance,nPNA). Glycated hemoglobin, fasting blood glucose, Nt-pro BNP, weekly urea clearance index (Kt/V), weekly creatinine clearance (Ccr), and oral glucose tolerance test (peritoneal equilibration test, PET)
Security assessment	Safety indicators: patient blood pressure, ultrafiltration volume, urine volume, Nt-pro BNP, Kt/V, Ccr, PET, adverse event monitoring.

statistical analysis	**analytic set** Full analysis set (Full Analysis Set, FAS): All with at least one exposure subjects studied for treatment. This analysis set will be used primarily for the analysis of baseline data. Set of Safety Analyses (Safety Analysis Set, SS): At least one study was accepted all subjects treated and with a record of safety after medication. Effectiveness Analysis Set (Effectiveness Analysis Set, EAS): All subjects included received at least one study treatment and had at least one post-treatment observation subjects for the evaluation of the effectiveness of the intermediate point. **statistical analysis technique** Continuous variables will be statistically described according to the data distribution, including number of cases (non-missing), mean, standard deviation, median and quartiles, maximum and minimum values. Calculate the number and percentage of each category of categorical variables. Main endpoint: Descriptive analysis was used to summarize baseline, post-treatment 6 months albumin and prealbumin measurements, and the difference in change from baseline of enrolled subjects. Paired t-tests were used to test for differences before and after treatment, and multiple problems were controlled by Hochberg method. Secondary endpoints: Descriptive analysis will be used to summarize the baseline, three months post-treatment, and six months post-treatment nutritional status, metabolic status, residual renal function, and trends in dialysis adequacy for enrolled subjects, with graphical presentations; Tests for changes relative to baseline: For continuous variables, paired t-tests or Wilcoxon's signed-rank test will be used to compare pre-and post-treatment differences based on data distribution; for categorical

	variables, McNemar-tests will be used to compare the behavior before and after. Safety analysis: Descriptive statistics were used to summarize adverse events and adverse reactions, drug-related treatment measures, outcomes, and severity classification. Subgroups were used if necessary(For example, whether dialysis is adequate or heart failure) stratified analysis of data was performed. Exploratory analysis: patients were divided into adequate and inadequate groups according to baseline $Kt/V \geq 1.7$. The improvement of nutritional indicators in different subgroups was analyzed.

catalogue

1. Research background

Peritoneal dialysis is a treatment method that uses the peritoneum as a semipermeable membrane. By injecting dialysate into the abdominal cavity, metabolic waste and excess water in the blood are allowed to permeate and diffuse into the dialysate, which is then drained from the body. This process helps remove toxins from the body and regulate electrolyte balance. Peritoneal dialysis has several advantages, including ease of operation, no need for an intravenous access, minimal impact on hemodynamics, the ability to preserve residual kidney function, and the flexibility to control treatment time and location. It is widely used as a substitute for kidney therapy in patients with end-stage chronic renal failure method.

However, long-term peritoneal dialysis can also lead to some adverse consequences, one of which is malnutrition. Malnutrition refers to a state where the nutrients ingested or absorbed by the body cannot meet its physiological needs, leading to dysregulation in the body's composition, function, or metabolism. Malnutrition is very common among patients undergoing maintenance peritoneal dialysis, with an incidence rate as high as 20% to 70%. The causes of malnutrition are numerous, including metabolic disorders due to reduced kidney function, decreased appetite, gastrointestinal symptoms, restricted diets, and medication use. Additionally, peritoneal dialysis itself can exacerbate the development of malnutrition its development is mainly manifested in: loss of proteins and amino acids: about 5 to 15g of protein is excreted daily through peritoneal dialysis fluid, of which about half is albumin. At the same time, about 10 to 20g of free amino acids are lost daily. These proteins and the loss of amino acids leads to negative nitrogen balance and decreased serum albumin levels.

Glucose absorption: Conventional peritoneal dialysis fluids contain high concentrations of glucose as a osmotic agent to increase the amount of water filtered. However, these glucose are also absorbed by the body, about 80-120g per day. These additional energy intake can lead to metabolic disorders such as obesity, hyperinsulinemia, insulin resistance and diabetes.

Inflammatory response: long-term peritoneal dialysis will cause chronic micro-inflammatory response, resulting in increased catabolic metabolism, reduced synthetic metabolism, decreased appetite, endocrine dysfunction and so on. At the same time, inflammatory response will also affect vascular permeability and hemodynamics, reducing ultrafiltration efficiency and the ability to remove toxins.

Malnutrition not only affects the quality of life of peritoneal dialysis patients, but also increases the risk of complications such as infection, cardiovascular events, and peritoneal failure, reducing survival rates. Therefore, improving the nutritional status of peritoneal dialysis patients,

It is one of the important measures to improve its prognosis and quality of life.

Currently, nutritional support strategies for peritoneal dialysis patients mainly include oral nutritional supplementation, enteral nutrition supplementation, parenteral nutrition supplementation, and modified peritoneal dialysate. Among these, modified peritoneal dialysate refers to adding beneficial components such as amino acids, ketones, and low-osmolarity agents to conventional glucose-containing peritoneal dialysate. This reduces glucose absorption, increases the clearance of water and toxins, provides essential amino acids and energy, and improves the body's metabolic function

Check your physical and nutritional status.

Amino acids are the fundamental units for protein synthesis and other important substances in the body, and they also serve as one of the key energy sources for oxidative metabolism. Amino acid peritoneal dialysate is a sugar-free and osmotic agent-free peritoneal dialysate containing 1.1% (11 g/L) free amino acids, with an amino acid composition similar to that found in human plasma. The main mechanisms of action of Amino acid peritoneal dialysis fluid are as follows: supplemental amino acids: Amino acid peritoneal dialysis fluid can provide amino acids to the blood through peritoneal diffusion, thus to compensate for the loss of protein and amino acids, increase serum albumin level, improve the body nitrogen balance and nutritional status.

Providing Energy: Amino acid peritoneal dialysate can serve as a sugar-free osmotic agent, moving water from the blood to the dialysate through osmotic pressure differences, thus achieving ultrafiltration. At the same time, amino acids can be absorbed by the body and participate in energy metabolism, providing about 40kcal of energy daily. This not only reduces the need for high-concentration glucose. Sugar dependence can also avoid the metabolic disorder caused by excessive absorption of glucose.

Metabolic Regulation: Amino acid peritoneal dialysis fluid can influence the secretion and activity of various hormones and cytokines in the body, thereby regulating metabolism. For example, amino acids can stimulate the secretion of insulin, glucagon, growth hormone, and insulin-like growth factor-1, promoting glucose utilization and protein synthesis; amino acids can also inhibit the secretion of tumor necrosis factor- α and interleukin-6, etc., inhibits inflammatory response and protein breakdown.

Amino acid peritoneal dialysate, as an improved version of peritoneal dialysate, has been clinically applied and studied in many countries and regions both domestically and internationally. Currently, numerous studies have confirmed the beneficial effects of amino acid peritoneal dialysate on the nutritional status of patients undergoing maintenance peritoneal dialysis [1-10]. For example, Sun Bin [1] et al. investigated the impact of amino acid peritoneal dialysis on the dialysis efficiency and nutritional status of peritoneal dialysis patients. The results showed that amino acid peritoneal dialysis can increase serum albumin levels, reduce urea nitrogen, uric acid, and blood phosphorus levels, and elevate hemoglobin levels, thereby improving the nutritional status of patients. Sun Yuling[3] et al. compared the effects of amino acid peritoneal dialysate and traditional glucose peritoneal dialysate on peritoneal mesothelial cells, finding that amino acid peritoneal dialysate better maintains cell viability, adhesion function, and protein synthesis. Faller[6] et al. treated peritoneal dialysis patients with optimized 1.1% amino acid peritoneal dialysate for 3 months and observed significant increases in serum albumin and transferrin levels. Jones [7] et al. found that compared to glucose dialysate, amino acid dialysate can improve albumin, prealbumin, and transferrin levels in malnourished peritoneal dialysis patients, and also observed improvements in muscle nutrition indicators. Delarue[9] et al. studied the impact of amino acid dialysate on creatine metabolism and found that amino acid dialysate can stimulate creatine release and increase protein synthesis. Li[10] et al. conducted a 3-year randomized controlled study, and the results showed that long-term use of amino acid dialysate can improve the nutritional status of peritoneal dialysis patients, especially for female patients.The above studies show that amino acid peritoneal dialysis fluid can effectively improve the nutrition of patients with maintenance peritoneal dialysis.

The state of temperament and metabolism promotes its growth and development and physical improvement. However, a meta-analysis in 2021 [13]comprised a review of 6,945 abstracts, including 14 studies (9 randomized and 5 non-randomized), concluded that amino acid peritoneal dialysate may not alter anthropometric indicators, the impact on serum albumin is uncertain, and the estimated differences are unlikely to have clinical significance. However, due to the low quality of evidence, these findings should be interpreted with caution. Based on the above meta-analysis, robust research is needed to address the limitations in the evidence. Therefore, we propose a multicenter, open, prospective, self-controlled clinical study aimed at observing the effects of amino acid

peritoneal dialysate on the nutritional status of patients undergoing maintenance peritoneal dialysis, as well as its safety assessment, with a view to promoting its clinical application

The application provides stronger evidence. The characteristics of this study are as follows:

Multicenter: This study will be conducted in five different regions of Guangdong province to improve the study its universality and representativeness.

Open: This study will not have a placebo or control group, but will use a self-control design, that is, each subject will be compared with the observation indicators before and after receiving amino acid peritoneal dialysis treatment to reduce individual differences and the influence of interfering factors.

Prospective: A detailed study protocol will be developed before the formal start of the study and will be carried out in accordance with the protocol. Record, report and other work to ensure the quality and credibility of the research.

Self-control: This study will use a self-control design, that is, each subject will receive amino acid peritoneal dialysis. The comparison of observation indicators before and after exudation therapy was carried out to reduce the influence of individual differences and other interfering factors.

2. Research objectives

2.1 Main objectives

The main purpose of this study was to evaluate the nutritional status of patients undergoing maintenance peritoneal dialysis with amino acid peritoneal dialysate the effect of improvement.

2.2 Secondary objectives

The secondary aim of this study was to explore the metabolic status of patients undergoing maintenance peritoneal dialysis with amino acid peritoneal dialysate effects on residual renal function, dialysis adequacy and safety.

2.3 Exploratory purposes

According to $Kt/V \geq 1.7$, patients were divided into dialysis adequate and non-dialysis adequate groups, and the effects of amino acid peritoneal dialysate on the nutritional status of patients with dialysis adequacy were explored; according to Nt-pro BNP levels, patients

were divided into non-heart failure groups and heart failure groups for further exploration safety of amino acid peritoneal dialysis fluid.

3. Test design

The experimental design of this study is as follows:

3.1 Research design

This study adopts a multicenter, open, prospective, and self-controlled design, where each participant serves as their own control before and after receiving amino acid peritoneal dialysis fluid treatment, to compare changes in their nutritional status. This study does not set up a placebo or control group, as amino acid peritoneal dialysis fluid is already on the market, with its efficacy and safety proven, and there are no equivalent alternatives. The primary objective of this study is to observe the nutritional improvement effects and safety assessment of amino acid peritoneal dialysis fluid for malnourished peritoneal dialysis patients. Specific techniques

The route is shown in Figure 1:

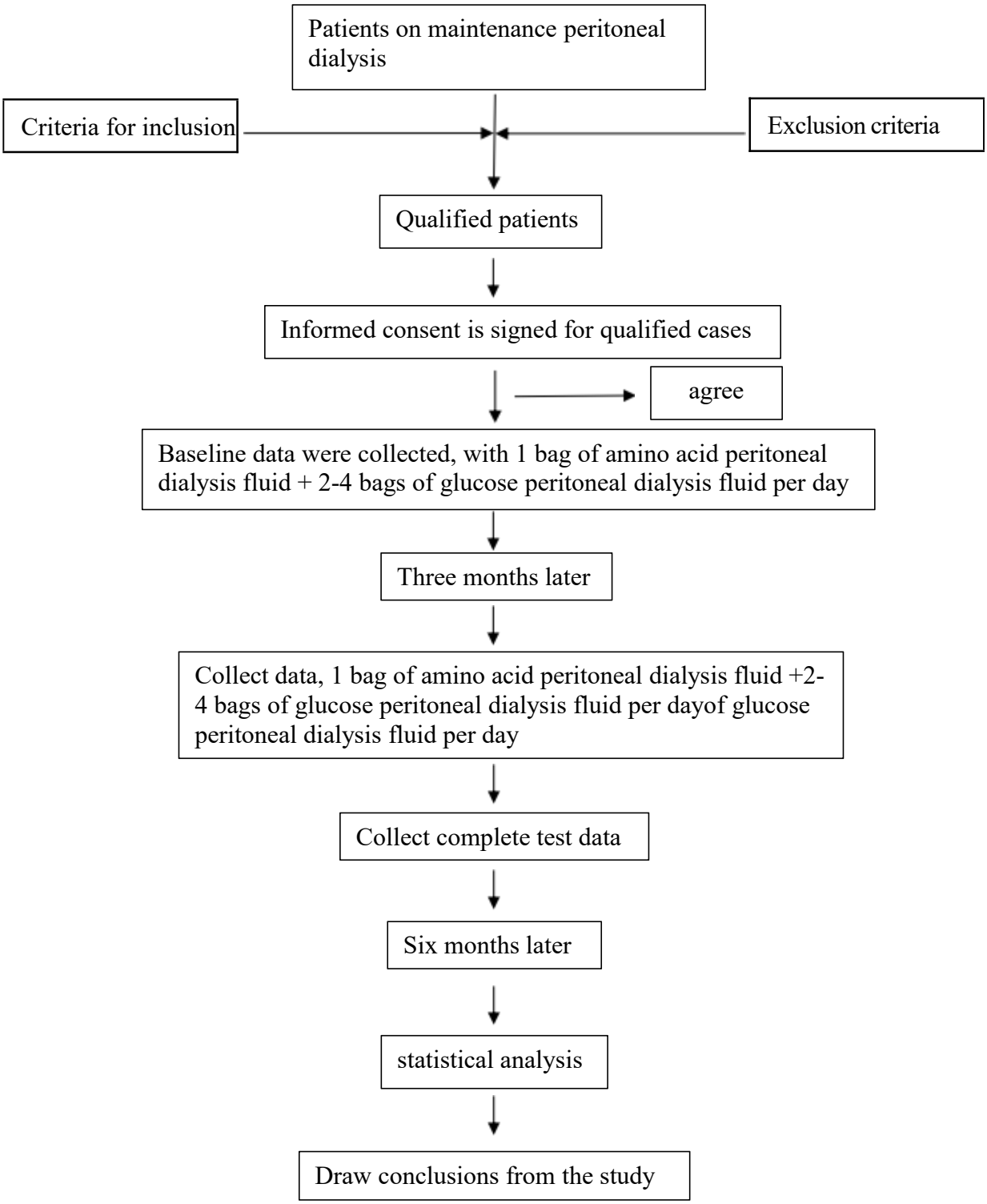

Figure 1. Technical route

3.2 Study endpoints and evaluation criteria

3.2.1 Main end indicators

The primary endpoint of this study was the improvement of nutritional status of subjects after 3 months and 6 months of treatment, it includes the following two indicators:

1) Serum albumin (g/L): the change value of serum albumin compared with baseline at 3 months and 6 months after treatment (Δ serum albumin);

2) Prealbumin (mg/L): the change value of prealbumin at 3 months and 6 months after treatment. The change value of prealbumin compared with the baseline after month (Δprealbumin);The treatment was considered effective if the difference in change from baseline for any of the above indicators was statistically significant.

3.2.2 Secondary endpoints

The secondary endpoint of this study was other relevant indicators of the subjects at 3 months and 6 months after treatment

The body is as follows: Mass (kg): The change in mass of the subject compared to baseline at 3 months and 6 months(Δ Body mass); BMI (kg/m^2): (Δ of the change in BMI of the subject compared to baseline at 3 months and 6 months BMI); CI: CI change value of the subject at 3 months and 6 months compared with baseline (ΔCI);

- Waist circumference and grip strength (cm/kg): The changes in waist circumference and grip strength compared with baseline at 3 months and 6 months were measured by a tape measure to measure the circumference of the narrowest part of the subject. The maximum grip strength of the subjects was measured with a grip strength gauge;

- Arm muscle circumference (cm): The change in arm muscle circumference (Δ arm muscle circumference) of the subjects compared with baseline at 3 months and 6 months was measured by a tape measure at the midpoint of the subject's upper arm and according to the formula

The calculated upper arm muscle circumference = arm circumference (cm) 0.3142 × triceps skinfold thickness (mm);

ΔnPCR (g/kg/d): nPCR change values of subjects at 3 months and 6 months compared to baseline(ΔnPCR);

ΔnPNA (g/kg/d): Changes in nPNA compared to baseline at 3 months and 6 months Value (ΔnPNA).

3) Metabolic status-Glycated hemoglobin (%): Glycated hemoglobin of the subjects at 3 months and 6 months compared to baseline White change value (Δ glycosylated hemoglobin) was measured by an automatic biochemical analyzer to measure the glycosylated hemoglobin of the subjects Hemoglobin levels.

4) Fasting blood glucose (mmol/L): Fasting blood glucose of the subjects at 3 months and 6 months compared with baseline

Change value (Δ fasting blood glucose) was measured by an automatic biochemical analyzer to measure the subject's fasting blood glucose level.

5) Indicators of residual renal function and dialysis adequacy

● Urine volume: the change in urine volume compared with baseline at 3 months and 6 months (Δ urine volume);

● Ultrafiltration: change in urine volume compared to baseline at 3 months and 6 months (Δ ultrafiltrationmeasure);

Kt/V: The change value of Kt/V compared with the baseline at 3 months and 6 months (ΔKt/V), calculated by the formula Kt/V= (V × Ln(C0/C1) + (V × UF)/C1)/V, where V is the body volume, C0 is the urea nitrogen concentration before infusion, C1 is the urea nitrogen concentration after outflow, and UF is the ultrafiltration measure;

Ccr (L/week): the change value of Ccr compared with baseline at 3 months and 6 months (Δ Ccr), calculated by the formula Ccr= (U × V)/P, where U is the concentration of urinary creatinine and V is the urine volume,P is serum creatinine concentration;

● PET: PET change values (ΔPET) at 3 months and 6 months compared to baseline

The formula PET= (D/P) × 100% was used to calculate the concentration of substances in the effluent D and P . The concentration of a substance in a filling liquid.

6) Capacity load index

Nt-pro BNP: Nt-pro BNP change values at 3 months and 6 months compared to baseline (ΔNt-pro BNP); the level of Nt-pro BNP in subjects was measured by electrochemiluminescence.

7) Safety endpoint (adverse event): assessed according to vital signs, physical examination, laboratory tests, etc.

3.2.3 Exploratory end point indicators

This study did not set up a separate exploratory endpoint indicator, for exploratory purposes of the indicator (nutritional status and safety comprehensive indicators) are the same as the primary and secondary endpoints.

3.3 Criteria for patient selection and exclusion

This study will be conducted in a multicenter design with five centers expected to enroll 140 subjects.

The inclusion, exclusion and withdrawal criteria of patients in this study are as follows:

3.3.1 Selection criteria

1. Select patients with uremia with malnutrition during the screening period and maintain peritoneal dialysis for at least 3 months. Malnutrition

The standard shall at least meet two of the following items:

(1) Serum albumin level <3.5g/dL (35g/L),

(2) Prealbumin <300mg/L,

(3) Subjective comprehensive nutritional assessment (SGA)> 7 points;

2. Blood urea nitrogen ≤ 38mmol/L;

3. The patient is between 18 and 75 years of age;

4. The patient signs an informed consent form.

3.3.2 Exclusion criteria

1. Allergy to any amino acid or excipient in this product;

2. Have had peritonitis more than once in the last 3 months; have had peritonitis or been hospitalized in the last 1 month;

3. Combine hyperthyroidism, systemic infection fever and other diseases of high catabolic state, as well as taking drugs that affect tissues

Metabolic drugs, such as corticosteroids;

4. Congenital amino acid metabolic defects, acute severe pancreatitis, severe hyperbilirubinemia;

5. Malignant tumor metastasis or diffusion, residual cancer after treatment, coagulation dysfunction, aplastic anemia, etc

Patients with serious diseases of other systems such as heart, brain and lung;

6. Kidney transplant may be accepted during the trial;

7. Active hepatitis B or C, cirrhosis, active liver disease, liver dysfunction or human immunodeficiency

The serum test for the defective virus (HIV) was positive.

8. Participants who have participated in other drug clinical trials within 3 months before enrollment;

9. Pregnant and lactating women;

10. A person who is not fit to cooperate;

11. No written informed consent was signed;

12. Inability or unwillingness to comply with the protocol approved by the investigator.

3.3.3 Exit criteria

Participants may withdraw from the study under any circumstances and should withdraw from the study in the following situations:

(1) The patient developed life-threatening complications;

(2) The occurrence of intolerable clinical symptoms related to the therapeutic drug;

(3) Pregnancy was combined during the study;

(4) The subject was assessed by the investigator as needing to withdraw from the trial;

(5) Unwilling to continue to participate in the study/informed consent withdrawal;

(6) Disappearance.

If the subject wishes to discontinue participation in the study, he/she will participate in the termination visit to complete the test items of the termination visit.

4. Research plan

4.1 Research phase and process

This study plans to enroll 140 patients with maintenance peritoneal dialysis who meet the inclusion and exclusion criteria, and is expected to be conducted in 5 centers. The study period for each subject is 6 months, and the entire study project will be completed in about 1 year. The study was divided into two phases: screening and treatment.

Screening period: Within 1 month before enrollment, patients who meet the inclusion criteria are initially screened, including physical examination, blood pressure

measurement, body weight measurement, BMI calculation, CI calculation, skinfold thickness measurement, waist circumference and grip strength measurement, upper arm muscle circumference measurement, SGA score, urine volume, ultrafiltration volume, biochemical and liver and kidney function tests, serum albumin, prealbumin, nPCR,nPNA, Kt/V and Ccr, Nt-pro BNP, hepatitis B related antigen and antibody, hepatitis C antibodies, HIV antibodies and other indicators were measured, and subjective nutritional score (SGA) and PET tests were performed. At the same time, explain the purpose, method, benefits and risks of this study to the patient and obtain his/her written informed consent. At the same time, inform the patient

The patient introduces the specific protocol and precautions of this study.

Treatment Phase: The treatment phase begins after enrollment. Each participant receives a regimen of 1 bag of amino acid peritoneal dialysis and 2-4 bags of glucose peritoneal dialysis fluid daily for 6 months (the amount of glucose peritoneal dialysis fluid is determined based on the treatment plan at the time of screening when the patient enters the study). The amino acid peritoneal dialysis fluid is provided by the research center, with the following composition: amino acids (15). The glucose peritoneal dialysis fluid is also provided by the research center, with the following composition: this product is a compound preparation, each 1L the composition of the solution is 1000mL, alanine 0.951g, arginine 1.071g, glycine 0.510g, histidine 0.714g, leucine 0.850g, lysine 1.020g, l-lysine hydrochloride 0.955g, methionine 0.850g, phenylalanine 0.570g, proline 0.595g, serine 0.510g, threonine 0.646g, tryptophan 0.270g, tyrosine 0.300g, ammonia 1.393g, sodium chloride 5.380g, Calcium chloride ($CaCl_2 \cdot 2H_2O$) 0.184g, Magnesium chloride (Mg, CL2· 6H2O]0.051g), Sodium lactate 4.480g, Ion concentration (mmol/L): Amino acids 87.16mmol/L, Sodium 132mmol/L, Calcium 1.25mmol/L, Magnesium 0.25mmol/L, Chlorine 105mmol/L, Lactate root 40mmol/L. The excipients of this product include hydrochloric acid and water for injection. This product is a glucose-free peritoneal dialysis solution, used as part of the peritoneal dialysis regimen

One part is used for the treatment of chronic kidney patients, especially suitable for peritoneal dialysis patients with serum albumin less than 35g/L.

The composition of glucose peritoneal dialysis fluid is shown in Figure 2:

Drug name	composition					ion concentration					osmotic pressure	pH	capacity
	C6H12O6·H2O	NaCl	C3H5NaO3	CaCl2·2H2O	MgCl·6H2O	Na	Ca	Mg	chloride	lactate			
Low Calcium Peritoneal Dialysis Solution(lactate-G1.5%)	1.5g	0.538g	0.448g	0.0183g	0.0051g	132.01	1.25	0.25	95.04	39.97	344	4.5-6.5	2000
Low Calcium Peritoneal Dialysis Solution(lactate-G1.5%)	2.5g	0.538g	0.448g	0.0183g	0.0051g	132.01	1.25	0.25	95.04	39.97	395	4.5-6.5	2000
Low Calcium Peritoneal Dialysis Solution(lactate-G4.25%)	4.25	0.538g	0.448g	0.0183g	0.0051g	132.01	1.25	0.25	95.04	39.97	483	4.5-6.5	2000

Figure 2. Composition of glucose peritoneal dialysis fluid

The daily use of 1 bag of amino acid peritoneal dialysis fluid is during the nighttime sleep period, while the daily use of 2-4 bags of glucose peritoneal dialysis fluid is during the daytime. The total daily infusion volume, each infusion volume, dwell time, and each excretion volume for each subject are adjusted by the researcher based on individual patient conditions and standardized prescriptions. During treatment, subjects should follow the researcher's guidance for daily life and dietary management, and regularly visit the research center for follow-up and examinations. In the third and sixth months of treatment, subjects should repeat the screening period

All evaluation items and any adverse events or serious adverse events are recorded.

The research process is shown in Table 1:

Table 1: Research process table

Evaluate projects	Screening period/baseline	stage of therapy					
		1 month	2 months	3 months	4 months	5 months	6 months
informed consent	√	×	×	×	×	×	×
Inclusion and exclusion criteria	√	×	×	×	×	×	×
Collect demographic data	√	×	×	×	×	×	×
Symptoms (loss of appetite, nausea, vomiting, abdominal distension , Infusion pain, edema, etc.)	√	√	√	√	√	√	√

Previous illness/treatment	√	×	×	×	×	×	×
Combination therapy with concomitant medication	√	√	√	√	√	√	√
allergic history	√	×	×	×	×	×	×
SGA	√	√	√	√	√	√	√
check-up	√	√	√	√	√	√	√
vital sign	√	√	√	√	√	√	√
Ultrafiltration volume	√	√	√	√	√	√	√
UPD	√	√	√	√	√	√	√
BMI	√	√	√	√	√	√	√
CI	√	×	×	√	×	×	√
skin-fold thickness	√	×	×	√	×	×	√
Waist circumference and grip strength, upper arm muscle circumference	√	×	×	√	×	×	√
Hepatitis B related antigen antibody, hepatitis C antibody, HIV antibody	√	×	×	×	×	×	×
Biochemistry and liver and kidney function (including serum albumin, Prealbumin), glycosylated hemoglobin White, fasting blood sugar	√	×	×	√	×	×	√
Nt-Pro BNP	√	×	×	√	×	×	√
nPCR	√	×	×	√	×	×	√

nPNA	√	×	×	√	×	×	√
Kt/V and Ccr	√	×	×	√	×	×	√
PET	√	×	×	√	×	×	√
adverse event	√	√	√	√	√	√	√

(1) Informed Consent: Before participants join this study, their written consent, either from the participant themselves or their legal representative, must be obtained. The informed consent form should include information on the purpose, design, process, risks, benefits, rights, and obligations of the study, as well as the participant's personal information and contact details. The informed consent form should be signed jointly by the researcher and the participant or their legal representative. It's kept in the research files.

(2) Collect demographic data: After the subject is selected for this study, basic information should be recorded, including name, gender,

Age, height, weight, BMI, etc. The formula for calculating BMI is: BMI= weight (kg) / height m2.

(3) Collect symptoms (loss of appetite, nausea, vomiting, abdominal distension, infusion pain, edema, etc.): After the subject is enrolled in this study, detailed questions should be asked about gastrointestinal related symptoms and edema, which should be recorded in CRF, and attention should be paid to whether there are causes related to this study or influencing factors.

(4) Collecting Past Medical History and Comorbidities: After a participant is enrolled in this study, their past medical history and comorbidities should be thoroughly inquired about. This includes all relevant internal and external medical conditions and surgical histories, as well as any medications currently being used or planned for use, and other treatments. The past medical history and comorbidities should be documented in the CRF, with attention to any factors relevant to this study

Or influencing factors.

(5) Inquiry of allergy history: After the subject is selected for this study, his/her allergy history should be inquired in detail, including allergen, allergic reaction and so on treatment methods, etc. Allergy history should be recorded in the CRF, and pay attention to whether there are factors or influencing factors related to this study.

(6) The improved SGA evaluation method was used. The higher the score, the worse the nutrition. Normal nutrition: 7 points; mild to moderate nutrition: 8-15 points; severe malnutrition: ≥ 16 points.

(7) Physical Examination: After the subject is enrolled in this study, a comprehensive physical examination should be conducted, including the head and face, skin system, lymph nodes, eyes, ears, nose, throat, mouth, respiratory system, cardiovascular system, abdomen, genitourinary system, musculoskeletal system, and nervous system. The results of the physical examination should be recorded in the CRF, with attention to any abnormalities or related issues clinical manifestation.

(8) Monitor vital signs: After the subject is enrolled in this study, their vital signs should be monitored regularly, including blood pressure (systolic and diastolic), heart rate (beats per minute), respiratory rate (breaths per minute), and body temperature (℃). Vital signs should be measured in a resting state using the same equipment and methods. The results of the vital signs should be recorded in the CRF, noting any abnormalities abnormal or abnormal related clinical manifestations.

(9) Record urine output and ultrafiltration: After the subject is enrolled in this study, their urine output and ultrafiltration should be regularly recorded to assess renal function and peritoneal function. Urine output is the average of the 24-hour urine collected at home, and the measurement of ultrafiltration at home should be taken before and after each session of peritoneal dialysis, using the same equipment and method. The results of urine output and ultrafiltration should be recorded and evaluated.The average value for the first 1 month is in the CRF and note any abnormal or abnormal related clinical manifestations.

(10) Measure skinfold thickness: After participants are enrolled in this study, their triceps skinfold thickness should be measured regularly to assess their nutritional and physical status. The measurement of skinfold thickness should be performed on the right upper arm at the triceps area using a standard skinfold caliper. The results of the skinfold thickness should be recorded in the CRF, noting any abnormalities or related clinical manifestations.

(11) Measure waist circumference, grip strength, upper arm girth, and CI: After participants are enrolled in this study, their waist circumference, grip strength, and upper arm girth should be measured regularly

Arm muscle circumference and CI to assess their nutritional and physical status. The waist circumference measurement should be taken at the level of the lower edge of the diaphragm,

And use a soft ruler. Grip strength measurement should be taken between the thumb and index finger of the right hand, using a standard grip strength gauge. The formula for calculating CI is: CI= waist circumference (m) / {0.109 × [body weight (kg) / height (m) $^{1/2}$}. Waist circumference, grip strength, upper arm muscle

The results of the peritoneal and CI should be recorded in the CRF, noting any abnormalities or abnormal related clinical manifestations.

(12) Biochemical blood tests: After the subjects are enrolled in this study, regular biochemical blood tests should be performed, including ALT (alanine transaminase), AST (aspartate transaminase), total bilirubin, direct bilirubin, blood urea nitrogen or urea, total protein, albumin, creatinine, blood glucose, lactate dehydrogenase, K^+, Na^+, Ca^{2+}, Cl^-, etc., to evaluate their liver function, kidney function and metabolism

Level. The results of biochemical blood tests should be recorded in the CRF and note any abnormalities or abnormal related clinical manifestations.

(13) Detection of Nt-pro BNP: After the subjects were enrolled in this study, screening period and treatment at 3 months and 6 months Nt-The results of the pro BNP should be recorded in the CRF, noting any abnormalities or abnormal related clinical manifestations.

(14) Detection of nPCR and nPNA: After the subject is enrolled in this study, his/her nPCR and nPNA should be regularly tested to evaluate his/her protein catabolism rate and total protein nitrogen presentation rate. The results of nPCR and nPNA should be recorded in the CRF and noted whether there are any abnormal or abnormal related clinical manifestations.

(15) Calculate Kt/V and Ccr: After the subject is enrolled in this study, Kt/V and Ccr should be calculated regularly to evaluate his/her dialysis efficiency and residual renal function. The results of Kt/V and Ccr should be recorded in the CRF, and attention should be paid to any abnormalities or abnormal related conditions clinical manifestations.

(16) Conduct PET testing: After subjects are enrolled in this study, regular PET tests should be conducted to evaluate their peritoneal dialysis material transport characteristics. The PET testing method follows the standard PET (Standard PET) proposed by Twar dowski. Measure the glucose concentration in the effluent and compare it with that in the infused fluid to calculate the D/P ratio and the D/D0 ratio. Based on the D/P ratio and the D/D0 ratio, subjects are categorized into four types: high transport, high average transport, low average transport, and low transport. The results of the PET testing should be

recorded in the CRF, noting any abnormalities or differences common associated clinical manifestations.

(17) Adverse events: The recording time is from the start of treatment to the end of survival follow-up, and only AE related to this study is collected,Including adverse events of special concern.

4.2 Data collection

4.2.1 Screening period

During the screening period, the following observations were performed on patients who met the inclusion criteria:

Informed consent: Explain the purpose, method, benefits and risks of this study to the patient, and obtain his/her written informed consent.

Inclusion/exclusion criteria: Check whether the patient meets the inclusion and exclusion criteria.

Past history/comorbidities/treatment: Record the patient's past history, comorbidities and treatment.

Comprehensive Subjective Nutritional Assessment (SGA): Using the improved method of SGA assessment in the 2010 version of The Standard Operating Procedures for Peritoneal Dialysis, patients were comprehensively assessed for nutritional status, including weight change, appetite change, gastrointestinal symptoms, activity ability and complications, physical examination, etc., and patients were divided according to the scoring results. There are three categories: normal nutrition (A), mild malnutrition (B) or severe malnutrition (C).Physical examination: Measure the patient's height, weight, blood pressure, heart rate, respiratory rate and other indicators, and calculate

BMI (BMI= body mass / height 2 (kg/m2)).

Blood pressure measurement: Use standardized methods and equipment to measure the patient's systolic and diastolic blood pressure and record itaverage value.

Body weight measurement: Use an electronic scale to measure the dry weight of the patient and record the value.

BMI Calculation: Calculate the patient's BMI based on weight and height data, and record its value.

CI calculation: Use the tape measure to measure the patient's waist circumference, and calculate the patient's CI value (CI= waist circumference (m) / {0.109 × [body weight (kg)/ height (m)] $^{1/2}$}) according to the weight and height data, and record it numeric value.

Waist circumference and grip strength measurement: Use a tape measure to measure the patient's waist circumference and record its value. Use a grip strength gauge, according to the standard method, the grip strength of each patient's left and right hands was measured once and the average value was recorded.

Triceps skinfold thickness measurement: Use a skinfold thickness gauge and follow a standardized method on the right side of the patient the triceps, the thickness of the skin fold was measured and recorded.

Arm muscle circumference measurement: Use a tape measure to measure the circumference of the patient's right arm, and calculate the patient's upper arm muscle circumference (= arm circumference (cm) 0.3142 x triceps skinfold thickness (mm)) according to the data of skinfold thickness, and record it the values.

Biochemical and liver and kidney function tests: venous blood samples were collected from patients, and serum creatinine, blood urea nitrogen, potassium, sodium, calcium, phosphorus, magnesium, bicarbonate, total protein, albumin, globule were measured by automatic biochemical analyzer

Indicators such as white, bilirubin, alanine transaminase, aspartate transaminase and alkaline phosphatase were measured and their values were recorded.

Serum albumin, prealbumin: venous blood samples were collected from patients and bromophenol green method and immunoturbidimetric method were used,

The serum albumin and prealbumin levels of patients were measured separately and their values were recorded.

Indicators such as nPCR,nPNA, Kt/V and Ccr were measured: according to the 2010 version of the Standard Operating Procedure for Peritoneal Dialysis, the protein catabolic rate nPCR (g/(kg · d)) and total protein nitrogen presentation rate of patients were calculated nPNA（g/(kg·d)）、 Kt/V 、 Ccr（L/1.73 m^2）。

Nt-pro BNP: According to the level of Nt-pro BNP, patients with Nt-pro BNP <11000pg/mL did not think there was heart failure or other factors affecting the level of Nt -pro BNP; patients with Nt-pro BNP ≥ 11000 pg/mL did not think there was heart failure or other factors affecting the level of Nt-pro BNP

The study process was closely monitored for possible factors such as heart failure or other factors affecting Nt-pro BNP levels.

Volume of urine, ultrafiltration: based on the patient's recent 1-month home monitoring records, record the average daily value.

PET test: Using standardized methods, patients were subjected to a peritoneal balance test (PET), which included the infusion of 2L of 2.5% glucose peritoneal dialysis fluid for 2 hours, followed by a 4-hour stay to measure creatinine and glucose concentrations. The infused fluid and the excreted fluid were then measured for weight, osmotic pressure, protein content, and creatinine content. Based on the results, the patient's ultrafiltration volume, urea nitrogen clearance rate, creatinine clearance rate, D/P creatinine ratio, and D/D0 creatinine were calculated

The ratio, D/P urea nitrogen ratio, D/D0 urea nitrogen ratio and other indexes were used to classify patients into high transport type (H)

There are four types: high average transport type (HA), low average transport type (LA) or low transport type (L).

4.2.2 During treatment

During the treatment period, each participant received a regimen of 1 bag of amino acid peritoneal dialysis and 2-4 bags of glucose peritoneal dialysis fluid daily for 6 months (the amount of glucose peritoneal dialysis fluid was determined based on the treatment plan at the time of screening when the patient entered the study). In the third and sixth months of the treatment period, participants should repeat all assessments from the screening phase and record any adverse events or serious adverse events. Monthly follow-up evaluations were conducted during the treatment period. Observe (infusion pain, abdominal distension), blood pressure, weight, urine volume, ultrafiltration.

5. Treatment plan

The treatment protocol of this study is as follows:

5.1 Research treatment

5.1.1 Treatment protocol

Each subject received a treatment regimen of 1 bag of amino acid peritoneal dialysis and 2-4 bags of glucose peritoneal dialysis fluid daily for 6 months (the amount of glucose peritoneal dialysis fluid was determined based on the treatment plan at the time of

screening when the patient entered the study). The amino acid peritoneal dialysis fluid was provided by the research center, with the following composition: amino acids (15). The peritoneal dialysis fluid was also supplied by the research center, containing the following components in each 1L solution: 1000 mL, alanine 0.951g, arginine 1.071g, glycine 0.510g, histidine 0.714g, isoleucine 0.850g, leucine 1.020g, lysine hydrochloride 0.955g, methionine 0.850g, phenylalanine 0.570g, proline 0.595g, serine 0.510g, threonine 0.646g, tryptophan 0.270g, tyrosine 0.300g, arginine 1.393g, sodium chloride 5.380g, calcium chloride (CaCL2 ·2H2O) 0.184g, magnesium chloride (Mg, CL2 · 6H2O]0.051g), and sodium lactate 4.480g, equivalent ion concentration (mmol/L): amino acid 87.16mmol/L, sodium 132mmol/L, calcium 1.25mmol/L,

Magnesium 0.25mmol/L, chlorine 105mmol/L, lactate 40mmo/L, the excipients of this product are hydrochloric acid and water for injection. This product is a peritoneal dialysis solution without grape, which is used as part of the peritoneal dialysis program for the treatment of chronic kidney patients

It is not suitable for peritoneal dialysis patients with serum albumin less than 35g/L.

The components of the glucose peritoneal dialysate are shown in Figure 2. The use of one bag of amino acid peritoneal dialysate is scheduled during nighttime sleep, while the use of 2-4 bags of glucose peritoneal dialysate is scheduled during daytime hours. The total daily infusion volume, each infusion volume, each dwell time, and each effluent volume for each participant are determined by the researchers based on the patient's condition

Individual circumstances and standardized prescriptions are adjusted.

5.1.2 Treatment dose adjustment

During the treatment, according to the changes of the patient's ultrafiltration volume, blood pressure, biochemical blood, nutritional status and other indicators, the researchers can adjust the dosage and frequency of treatment appropriately to ensure the patient's water and electrolyte balance and metabolic stability. Specifically, the adjustment principles are as follows:

If the patient develops signs of water retention such as weight gain, edema, and hypertension, the researcher can increase the frequency of amino acid peritoneal dialysis or increase the concentration of glucose peritoneal dialysis to increase ultrafiltration and reduce water Sub-daily intake.

If the patient shows signs of water loss such as weight loss, hypotension, and hypoglycemia, the researcher can reduce the number of times of amino acid peritoneal dialysis fluid or reduce the concentration of glucose peritoneal dialysis fluid to reduce the amount of ultrafiltration and increase water intake.

If the patient shows signs of elevated or decreased blood potassium, the investigator can administer drug therapy to replenish potassium, to maintain normal blood potassium levels.If the patient shows signs of elevated or decreased blood calcium, the investigator can adjust the patient's calcium and vitamin D. The dosage of the drug is to maintain the blood calcium level within the normal range.

If the patient shows a decrease in nutritional indicators such as serum albumin, prealbumin, nPCR, and nPNA, the researcher can increase the number of times or volume of amino acid peritoneal dialysis to provide more amino acids and energy, and give patients appropriate nutritional support and education.

5.2 Adjuvant therapy/combined medication

During treatment, in addition to the use of amino acid peritoneal dialysis fluid and glucose peritoneal dialysis fluid, the subjects should also

Continue with their original adjuvant therapy, including:

Nutritional support drugs: if the patient has been taking nutritional drugs before entering the study, continue the original nutritional drug treatment,

No additional nutritional support drugs were added after entering the study.

Antihypertensive drugs: adjust the type of antihypertensive drugs according to the patient's blood pressure level and ultrafiltration. The dose is used to keep blood pressure within the target range.

Antianemia drugs: erythropoietin is adjusted according to the patient's hemoglobin level and iron metabolism. The type and dose of EPO and iron supplements were used to improve anemia.

Calcium and vitamin D drugs: according to the patient's blood calcium, blood phosphorus, parathyroid hormone (PTH) and other indicators

Targets, adjust the types and doses of calcium and vitamin D drugs to prevent and treat renal bone disease.

Phosphorus binder: Adjust the type and dose of phosphorus binder according to the patient's blood phosphorus level and diet. Control blood phosphorus levels within the target range.

Anticoagulant drugs: adjust the type and dose of anticoagulant drugs according to the patient's coagulation function to prevent and treat thrombosis.

Other drugs: other necessary drug therapy, such as anti-infective drugs, is given according to the specific condition of the patient anti-heart failure drugs, anti-arrhythmia drugs, uric acid reduction.

5.3 Treatment compliance

During the treatment period, participants should use the amino acid peritoneal dialysate and glucose peritoneal dialysate correctly according to the instructions and prescriptions of the researcher, and record each infusion volume, retention time, and output. Participants should submit their daily treatment logs to the researcher for verification and storage. Participants should maintain good peritoneal dialysis techniques and hygiene habits to prevent infections and complications. Participants should regularly visit the research center for follow-up visits and examinations, and promptly report any adverse reactions or discomforts to the researcher. Participants should adhere to dietary, hydration, and exercise recommendations provided by the researcher and avoid using other drugs or treatments that may affect the results of this study. If a participant is unable to continue participating in this study for any reason, they should notify the researcher in a timely manner and explain the reasons for withdrawal follow.

6. Adverse events

6.1 Definition of adverse events

Adverse events (Adverse Event, AE) are any harmful medical events that occur during a clinical trial. Events, regardless of whether they have a causal relationship with the test drug. Adverse events include the following: Adverse reactions related to the test drug (Adverse Reaction, AR): refers to the normal use conditions. Any harmful medical event caused by the pharmacological action of the test drug or for other reasons. Adverse events not related to the test drug: any harmful medical event that occurs during a clinical

trial, However, it was scientifically determined that there was no causal relationship with the test drug.

Serious adverse events (Serious Adverse Event, SAE): refers to those that occur during clinical trials

Any harmful medical event, regardless of whether it has a causal relationship with the investigational drug, that results in one of the following outcomes:

Causing death;

Life-threatening (i.e., potentially fatal if not promptly intervened);

Hospitalization or extension of hospitalization is required;

Causing permanent or significant disability or impairment;

Causing congenital malformations or birth defects;

Major medical intervention (such as surgery, blood transfusion, etc.) is required.

6.2 Observation and handling of adverse events

In this study, all subjects should undergo regular safety assessments, including subjective patient reports (such as abdominal pain, bloating), blood pressure, ultrafiltration volume, urine output, Nt-pro BNP, Kt/V, Ccr, PET, and other indicators. Researchers should document all adverse events that occur during the clinical trial and observe and manage them. The principles of inspection and handling are as follows:

The investigator should ask the subject if he or she feels any discomfort and actively observe whether the subject has any abnormal symptoms present.

Researchers should record the name, time of occurrence, duration, severity, and trial of all adverse events information such as causality, treatment measures and outcomes of the drug should be filled in the adverse event report form.

Researchers should provide appropriate treatment and support measures according to the nature and severity of adverse events closely monitor the subject's condition.

Researchers should decide whether to continue use based on the causal relationship and impact of adverse events and trial drugs.The test drug or withdrawal from the study.

Researchers should report all adverse events that occur during clinical trials to the ethics committee and sponsor in a timely manner events and track and update them as required.

6.3 Criteria for judging the relationship between adverse events and tests

The causal relationship between adverse events and the test drug should be judged according to the following criteria:

Assured of relevance (Definitely Related): Adverse events are related to the pharmacological action of the investigational drug or a known adverse event

The results were consistent and other possible causes were ruled out.

Most likely related (Probably Related): Adverse event and pharmacological action of the investigational drug or known no The good response is consistent and other possible causes are unlikely.

May be related (Possibly Related): Adverse event is related to the pharmacological action of the investigational drug or a known adverse eventThere are some similarities in the reaction, but there are other possible reasons.

It is unlikely to be related (Unlikely Related): the adverse event is related to the pharmacological action of the investigational drug or is known. There was no clear similarity in the adverse reactions and there were other more likely causes.

Irrelevant (Not Related): The adverse event is completely unrelated to the pharmacological action of the test drug or a known adverse reaction. It does not match and there are other clear reasons.

6.4 Evaluation of adverse reactions

Adverse reactions (i.e., adverse events related to the investigational drug) should be evaluated according to the following criteria:

Mild (Mild): The adverse reaction is mild and does not affect the daily life and work of the subject, and no special treatment is required texture.

Moderate (Moderate): Moderate adverse reactions, affecting the daily life and work of subjects, requiring certain therapeutic or supportive measures.

Severe (Severe): The adverse reaction is serious and seriously affects the daily life and work of the subject, requiring urgent treatment rapid or specialized treatment or support measures.

6.5 Reporting of adverse events

All adverse events occurring during clinical trials shall be reported in accordance with the following requirements:

All adverse events should be filled in the adverse event report form within 24 hours after occurrence and 7 days after occurrence and report to the ethics committee and sponsor within days. All serious adverse events should be reported by telephone, fax, email, etc. within 24 hours after occurrence. Notify the ethics committee and the sponsor, and submit a written report within 7 days after the occurrence. All serious unexpected reactions (Serious Unexpected Adverse Reaction, SUSAR) related to the test drug should be reported to the National Food within 24 hours of occurrence by telephone, fax, email, etc. The drug administration shall submit a written report within 15 days after the occurrence. All serious unexpected adverse reactions unrelated to the test drug should be reported by telephone, fax or electronic means within 7 days of occurrence. Report to the State Food and Drug Administration by mail, etc., and submit a written report within 30 days after the occurrence.

7. Statistical considerations

7.1 Sample size calculation

This study is a post-marketing study, and a total of 140 subjects are planned to be included. The efficacy evaluation standard is 6 months of treatment

If the difference between the post-relative baseline change of Δ serum albumin or Δ prealbumin is statistically significant, it is considered

The treatment was effective. Based on the above hypothesis, a single sample self-preceding and following control design and a unilateral difference test were used

Quantity estimation formula:

$$n = \frac{(za + z\beta)\,\sigma 2^{2}}{\delta 2}$$

δ is the difference; σ is the standard deviation, which will be replaced by the sample size standard deviation.

The Hochberg method was considered to adjust for multiple endpoints, with the smallest test level $\alpha/2= 0.0125$ (one-sided) and power $(1- \beta) = 0.9$, based on the sample size estimates for different primary efficacy endpoints

count.

1) Based on Δ serum albumin: According to the literature, it is assumed that the baseline serum albumin before treatment is 27 g/L, and the serum albumin after 6 months of amino acid peritoneal dialysis treatment is 28.5g/L, δ is 1.5g/L, and the standard deviation is 4.5 g/L,

The required sample size for the calculation was 112.

2) Based on Δ prealbumin: According to the literature, it is assumed that the baseline prealbumin before treatment is 240 mg/L, the prealbumin 6 months after amino acid peritoneal dialysis treatment is 300mg/L, δ is 60mg/L, and the standard deviation is 80 mg/L, the required sample size for calculation is 23 cases.

In order to ensure that the final analysis of this study has enough sample size, considering the possible loss to follow-up, withdrawal, invalid data and other situations, the maximum sample size of 112 cases estimated based on the above two indicators will be increased by 20%

The dropout rate was expanded to a total sample of 140 cases.

7.2 analysis set

Full analysis set (Full Analysis Set, FAS): All subjects who received at least one study treatment.This analysis set will be used primarily for baseline data analysis.Safety Analysis Set (Safety Analysis Set, SS): Received at least one study treatment and was on medication. All subjects in the safety record. This data set will be used primarily for safety analysis.Effectiveness Analysis Set (Effectiveness Analysis Set, EAS): All subjects included received at least one study treatment and had valid evaluation data at at least one post-treatment observation time point. The analysis set will be used mainly for efficacy analysis.

7.3 stochastic

This study adopted the self-control design, that is, each subject first used conventional peritoneal dialysis fluid for 3 months. And the patients were given 6 months of intravenous albumin peritoneal dialysis. Therefore, randomization was not required for this study. Subjects were screened enrollment in the order of success.

7.4 General analysis considerations

Continuous variables will be statistically described based on the data distribution, including number of cases (non-missing numbers), mean, standard deviation, median and quartiles, maximum value, and minimum value. For categorical variables, the number of cases and percentages for each category will be calculated unless otherwise specified; missing cases will not be included in percentage calculations, and counts with zero cases will be displayed as "0". The distribution of participants, demographic characteristics, past medical history/comorbidities/treatment, and study endpoints will be provided statistical analysis summary.

7.5 Missing data

For participants enrolled in the study, researchers will make every effort to collect their data, especially data related to the primary endpoint. If a participant's efficacy data is missing for any reason, continuous variables will be handled using the last observation carry-forward method (Last Observation Carried Forward, LOCF), while categorical data will be processed according to actual circumstances or filled in through modeling. Missing data. Other processing methods are described in detail in the Statistical Analysis Plan (SAP).

7.6 Statistical analysis methods

7.6.1 Demographic and baseline status, compliance, medical history, and analysis of concomitant disease treatment

Descriptive statistics of demographic and baseline characteristics of enrolled subjects will be performed based on the FAS set.The demographic data and baseline characteristics of all subjects were listed.Descriptive statistics were performed for treatment compliance throughout the study period, and compliance levels were summarized (i.e., <80% Number and percentage of subjects (80% to 120% and>120%). Summarize the number and percentage of subjects with a history of disease and comorbidities/treatment categories.

7.6.2 Statistical analysis of the primary endpoint

Statistical analysis of the primary endpoint will be based on the EAS set, including primary analysis and sensitivity analysis.

1) Main analysis:

1) Descriptive analysis will be used to summarize the baseline, post-treatment 6 months albumin and pre-protein measurements of the subjects in the group, as well as the difference in change from baseline; LOCF will be used to process the data on major efficacy loss

The paired t-test was used to test the difference before and after treatment.

2) Sensitivity analysis: The robustness of the analysis results will be evaluated by considering different missing data processing situations. The missing data of the main efficacy after treatment will be filled with the mean and median of the complete observation data respectively method, hypothesis testing is the same as the main analysis.

7.6.3 Statistical analysis of secondary endpoints

Based on the EAS dataset, descriptive analysis will be used to summarize the baseline characteristics of enrolled subjects, changes in nutritional status, metabolic state, residual renal function, and trends in dialysis adequacy at 3 months and 6 months post-treatment, with graphical presentations. For the comparison of changes from baseline: continuous variables will be compared using paired t-tests or Wilcoxon-signed rank tests based on data distribution; for categorical variables, McNemar-tests will be used compare yourself before and after.

7.6.4 safety analysis

Based on the SS set, all AE will be summarized by descriptive analysis. In addition, they will be summarized separately by drug correlation, drug-related treatment measures, outcomes and severity. If necessary, they will be summarized by subgroup (e.g

Data were stratified according to whether dialysis was adequate or heart failure).

Summarize the changes of vital signs, laboratory tests and ECG results of each group relative to baseline, the results with clinical significance after baseline and all test results were listed.

7.6.5 Exploratory analysis

Patients were divided into adequate and inadequate groups according to baseline Kt/V ≥ 1.7, and the improvement of nutritional indicators in different subgroups was studied

Analysis of variance. If applicable, differences in the improvement of nutritional indicators will be tested based on different groups of baseline.

7.7 Multiplicity issues

This study involves multiple primary efficacy endpoints: Δserum albumin and Δprealbumin. If any one of these endpoint indicators is statistically significant, the trial is considered effective, which can lead to an inflated overall false discovery rate (FWER). The Hochberg method is planned to control FWER: the P-values of the two tests are ranked from largest to smallest, denoted as p(1)> p(2), and then compared with the corresponding ai in descending order. First, the hypothesis H(01) corresponding to the largest r-value p(1) is tested. $\frac{\alpha}{2}$If p(1) <a1 (a1 = a, one-sided 0.025), all null hypotheses are rejected, and the test is stopped; if the one-sided test p(1) ≥ 0.025, H(01) is not rejected, and the next test continues; the test level a2 = (one-sided 0.0125) continues to test H(02). Statistical tests for other indicators are not the primary objective and are not considered multiple adjustments.

8.Ethical norms

The ethical guidelines for this study are as follows:

8.1 Ethical review

This study must be reviewed and approved by the ethics committees of each center before it officially begins, and must comply with relevant laws, regulations, and guidelines such as the World Medical Association's Helsinki Declaration and the National Medical Products Administration's Quality Management Standards for Clinical Trials. All documents and materials of this study, including the trial protocol, informed consent form, drug instructions, adverse event report forms, etc., should be submitted to the ethics committee for review. If any significant changes or unexpected events occur during the

study, they should be promptly reported to the ethics committee, and reapply for review and approval.

8.2 Informed consent

This study must provide participants with a detailed informed consent form before recruitment. The researcher or their authorized personnel should explain the purpose, methods, duration, benefits, risks, rights, obligations, confidentiality, and withdrawal procedures of the study to the participants both orally and in writing, and answer any questions or concerns raised by the participants. Participants must sign the informed consent form after fully understanding and voluntarily agreeing to participate, with a copy retained. The informed consent form should be written in the language and cultural context of the participants, using simple and clear language as much as possible. If the participant is a minor or unable to sign the informed consent form, it should be signed by their legal guardian or authorized representative the person in charge shall sign on behalf of the subject and obtain the consent of the subject himself.

8.3 Protection of subjects' rights and interests

In this study, the following principles should be observed in protecting the rights and interests of subjects:

Respect the autonomy of the subject: The subject has the right to choose whether or not to participate in this study and when to withdraw from this study without any coercion or influence. After withdrawing from this study, the subject still has the right to receive appropriate medical care and care bosom.

Protection of the welfare of subjects: Subjects have the right to benefit from this study, including improving their health status, improving their quality of life, and acquiring new medical knowledge. Subjects also have the right to benefit from this study compensation for damages, including medical expenses, transportation expenses, loss of earnings, etc.

Maintain the dignity of the subject: The subject has the right to keep his or her personal information and medical data confidential and not disclosed

Disclosure or abuse. Participants also have the right to avoid any discrimination or humiliation arising from their participation in this study.

8.4 Data quality and security supervision

In order to ensure data quality and security, the following principles should be observed in this study:

Ensure the authenticity of data: Researchers should collect, record, verify, store, and report all research data accurately, completely, and promptly according to the trial protocol and operating procedures. There must be no falsification, omission, alteration, or concealment. Researchers should use a standardized data entry form and fill it out with a black ink pen. If corrections are needed, a line should be drawn through the original content, followed by a signature and date. The use of correction fluid or similar substances is strictly prohibited correction bands, etc.

Ensure the validity of data: Researchers should regularly conduct quality control and assurance for research data, checking the integrity, consistency, accuracy, and reliability of the data, and promptly correcting or supplementing any errors or missing data. Researchers should accept data monitoring and auditing from sponsors or their authorized institutions, and cooperate in providing all necessary information for the study relevant documents and information, and accept their verification and validation of the data.

Ensure data security: Researchers should properly manage all research data to prevent loss, damage, leakage, or misuse. They should protect electronic data using passwords or encryption methods and back it up regularly. Researchers should archive and preserve paper data according to legal requirements and the ethics committee's guidelines limit their access.

9. Quality assurance

The quality assurance of this study is as follows:

9.1 Requirements for project leader

The project leader should have relevant knowledge and experience in clinical research and be able to effectively organize and manage the study all aspects of the research to ensure the scientific, compliance and quality of the research.

The project leader shall be responsible for the formulation and revision of the test plan and provide detailed instructions to the researchers in each center. Provide standardization and training guidance to ensure the uniformity and standardization of this study. The project leader shall be responsible for effective communication with the

sponsor, ethics committee, supervisory agency and statistical agency, report the progress and results of this study in a timely manner, and deal with any problems and risks that may arise.The project leader shall be responsible for supervising the researchers of each center to comply with the trial protocol and ethical norms, regularly reviewing and providing feedback on the data of each center, and recording and correcting any violation or deviation from the trial protocol the first month of the lunar year.The project leader shall be responsible for the preservation of all documents and materials of the study, and summarize and conclude after the completion of the study appraise.

9.2 Requirements for researchers

Researchers should have relevant knowledge and experience in clinical research, and be able to follow the trial protocol and operating specifications. To carry out all tasks of this study in a correct, complete and timely manner to ensure the reliability and effectiveness of this study. Researchers shall sign a training confirmation after receiving training from the project leader or his authorized agency and obtain it After approval by the ethics committee, subjects were recruited and the study was conducted.

Researchers should provide a detailed informed consent form to the subject before recruiting the subject, which shall be signed by the subject and a copy shall be kept. Researchers should respect the autonomy, welfare and dignity of the subject and protect the subject confidentiality of personal information and medical data.

Researchers should use a standardized data collection form (CRF) and fill it out with a black ink pen. If corrections are needed, a line should be drawn over the original content, and a signature along with the date should be noted; no correction fluid or correction tape should be used. Researchers should regularly send the CRF to the project leader or their authorized institution and keep a copy on file stem or root of plants.

Researchers should follow up and evaluate subjects regularly according to the protocol, and record all events and outcomes related to the study. Researchers should report any adverse events or serious adverse events in a timely manner, and root according to the instructions of the project leader or its authorized agency, carry out corresponding processing and tracking.

Researchers shall comply with the supervision and audit of the project leader or its authorized agency, and cooperate in providing all relevant research review relevant documents and data, and accept their verification of the data.At the end of this study, the researchers should submit all CRF, informed consent form, adverse event report form and

other documents and data shall be archived and preserved, and summarized and evaluated according to the requirements of the project leader or its authorized agency.

9.3 Quality control of treatment plan formulation and implementation

The treatment plan shall be formulated by the project leader or its authorized agency, and shall be submitted to the trial protocol and operating specifications. Researchers at each center provide detailed guidance and training to ensure uniformity and standardization of treatment plans. The treatment plan should include the name, specification, dosage, frequency, route and duration of the treatment drugs. Make appropriate adjustments and optimizations according to the specific conditions of the subjects. The therapeutic drugs shall be provided by the sponsor or its authorized agency and stored in accordance with the prescribed conditions and methods. Storage, transport, distribution, use and recovery to ensure the quality and safety of therapeutic drugs. The use of therapeutic drugs should be carried out by the investigator or his authorized personnel in accordance with the treatment plan and operating specifications, record, verify, monitor and evaluate, and report in a timely manner any events and outcomes related to the treatment drugs.

10. Data processing and data preservation

10.1 Case Report Form (CRF)

The Case Report Form (CRF) is a standardized table that records all data and information of the subject throughout the study process. The CRF should be promptly, accurately, and completely filled out by the investigator or their authorized personnel after each visit or observation, with the date signed. The CRF should be designed and compiled according to the observation items and time points specified in the trial protocol, including baseline data, follow-up data, efficacy evaluation, safety evaluation, adverse event records, etc.

The CRF should follow the following principles:

The CRF should be filled out in Chinese or English. If other languages are required due to special circumstances, corresponding translations should be provided

The translation shall be verified and signed by the researcher or his authorized personnel.

The CRF should be filled out with a black ink pen or signature pen and not with a pencil or any other colored pen.

The CRF should be clear, neat and easy to identify. There should be no alteration, cancellation or covering. If there is any error or omission, a horizontal line should be drawn on the original data and the correct data should be written next to it, and the person who filled in the form should write it date of signature. Do not use correction fluid or correction tape to modify the data.

The CRF shall reflect the authenticity and integrity of the original data, and no data shall be added, deleted or modified at will. If there is any data, any change or supplement shall be explained and signed by the investigator or his authorized person with the date.The CRF should be filled in in time according to the time point specified in the trial protocol, and should not be delayed or filled in in advance. If the data are delayed or missing due to special circumstances, the reason should be explained and signed by the investigator or his authorized person on the date.The CRF should be filled out by the investigator or his authorized person in person and should not be entrusted to others. If more than one person is involved in filling out the CRF. Write, indicate your name and responsibilities on the CRF, and sign the date of responsibility in each section.The CRF should be stored in a safe, dry and fireproof place after each filling, and should not be lost or damaged. If there is an electronic version of the CRF, appropriate measures should be taken to protect the security and confidentiality of the data, so as to prevent the data from being tampered with or leaked reveal.

10.2 Establishment of databases

In order to ensure the quality and reliability of the data, a special database system will be established for CRF data entry, verification, analysis and management. The database system should have the following functions:

The database system should have a reasonable structure and standard format, can effectively store, retrieve and process data occupy. The database system should have a good user interface and operation guide, can easily enter data, repair modify, query and export. The database system should have strict permission control and authentication mechanism, only authorized users are allowed to access and operate data and record user operation logs. The database system should have effective data verification and quality

control functions, can detect and correct the data errors, anomalies and inconsistencies are generated and corresponding reports and alerts are generated. The database system should have perfect data backup and recovery functions, and can prepare data regularly or at any time. In addition, data loss or damage can be recovered in time. The database system should have flexible data analysis and reporting functions, which can be based on research objectives and statistical methods, perform descriptive and inferential analysis of the data and generate corresponding tables and graphs.

The establishment and maintenance of the database system is the responsibility of professional data managers, whose main work includes: Design and establish the database system according to the test plan and CRF content, and conduct testing and verification. Enter, check, verify and clean the data in CRF to ensure the accuracy and integrity of the data. Perform regular or irregular maintenance and update of the database system to ensure the security and stability of data. Provide data query, export, analysis and reporting services at the request of researchers or monitors. After the study is completed, the database system shall be sealed and relevant documents and records shall be kept.

10.3 Preservation of information

All data involved in this study, including CRF, database, raw data, analysis data, statistical report, informed consent, ethics approval, trial protocol, trial drug records, etc., shall be in accordance with national laws and regulations

The principle of proper preservation and management shall be followed. The preservation of the data shall follow the following principles:

The data should be kept in a safe, dry and fireproof place to prevent loss or damage. If there is electronic data, appropriate measures should be taken to protect the security and confidentiality of the data and prevent the data from being tampered with or leaked. The data shall be kept for no less than 15 years according to the prescribed time limit. If there are special circumstances, the period may be extended or shortened. The retention period should be approved by the ethics committee and justified. The data shall only be consulted or used by authorized personnel, and the time, purpose and results of consultation or use shall be recorded. If the data need to be provided to a third party, the consent of the subject, the investigator, the sponsor and the ethics committee shall be obtained,

And sign the corresponding agreement.At the end of the retention period, the data shall be destroyed or transferred in accordance with the prescribed procedures. If the data

is to be destroyed, it shall be ensured that the data is completely destroyed and cannot be recovered or identified. If the data is to be transferred, it shall be ensured that the data is intact transfer, and the receiving party shall bear the responsibility of preservation and management.

11. Clinical research sponsor

Peritoneal dialysis Center, Gaozhou People's Hospital.

12. Work progress

The progress of the study is shown in Table 2 below:

Table 2. Work schedule

job content	leading official	start time	terminal time	remarks
Design and revision of the test plan	investigator	April 1, 2023	September 30,2023	-
and approval of the ethics committee	investigator	October 1, 2023	October 30,2023	-
Application and procurement of test drugs	investigator	October 1, 2023	October 30,2023	-
nd production of case report form (CRF)	ta management personnel	April 1, 2023	September 30,2023	-
Training and assessment of researchers	investigator	September 30,2023	October 30,2023	-
Screening and enrollment of subjects	investigator	November 01,2023	April 30,2024	-
Treatment and follow-up of subjects	investigator	November 01,2023	October 30,2024	-
Collection and verification of CRF	ta management personnel	October 30,2024	November 30,2024	-
Data entry and cleaning	ta management personnel	November 30,2024	December 30,2024	-
Data analysis and reporting	data management Personnel/research The investigator	January 1, 2025	January 30,2025	-
Publication and dissemination of research results	investigator	February 1, 2025	-	-

Preservation and destruction of data	investigator / data management personnel	-	-	Press illuminate instrument for drawing circles Fix defend Exist 15year

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