Intestinal Microbiota Transplantation for Nonalcoholic Fatty Liver Disease (NAFLD)

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1.Method

Intestinal microbiota transplantation(IMT) refers to make fecal from the health into a suspension of microbes through an intelligent bacteria processing system, and then infuse the suspension into the gastrointestinal tract of patients through naso intestinal tube, gastroscope, enteroscope or capsule intake which can reconstruct intestinal microbiota and play the role of treatment without obvious side effect.

2.Plan

1)Patient recruitment

Inclusion Criteria:

- subjects with NAFLD(nonalcoholic fatty liver disease)
- aged 18-65
- 24≤BMI
- liver/spleen (L/S) ratio no more than 0.7 by CT scan

Exclusion Criteria:

- Alcoholic liver disease (ALD), chronic hepatitis C, autoimmune liver disease, Wilson's disease
- Drug treatment (tamoxifen, amiodarone, sodium valproate, methotrexate, glucocorticoids, etc.),total parenteral nutrition, inflammatory bowel disease, hypothyroidism, Cushing's syndrome, beta lipoprotein deficiency, IR related syndromes (lipid wasting diabetes mellitus, Mauriac syndrome), gastrointestinal surgery
- Hepatocellular carcinoma (HCC), biliary tract diseases and taking or taking chinese and western medicines that can lead liver enzymes elevation in the near future.
- Moderate and severe renal injury (serum creatinine>2mg/dL or 177mmol/L), moderate and severe chronic obstructive pulmonary disease, severe hypertension, cerebrovascular accident,congestive heart failure, unstable angina pectoris.
- Antibiotics treatment in 7 days before recruited and unwilling to stop it, long-term lipid-lowering drugs, antidiabetic drugs and other liver protecting drugs treatment
- Antibiotics, other probiotics, gastrointestinal motility drugs and other preparation that may influence intestinal microbiota treatment
- Other serious diseases that may interfere the recruitment or affect the survival, such as cancer or acquired immune deficiency syndrome
- Mentally or legally disabled person
- Preparing for pregnancy
- Medical or social condition which in the opinion of the principal investigator would interfere with or prevent regular follow up articipating in other clinical trials.

Recruit the patients who meet the inclusion criteria, and fail to meet the exclusion

criteria. Introduce this clinical trial to the patients and obtain the informed consent. Assess the condition of the disease.

2)Arms and Interventions

Randomly divided the patients into experimental arm and control arm and intervene them as described in the following table.

arms	Assigned interventions
Experimental: IMT 30 non-alcoholic fatty liver disease（NAFLD） patients will be recruited for the study, which involved a 6 times intestinal microbiota transplant(IMT) and the time interval is generally 2 weeks. Interventions: Procedure: Intestinal Microbiota Transplantation	intestinal microbiota transplant intestinal microbiota transplantation Participants in Experimental group take 6 times IMT with 2-week intervals
Agents 30 non-alcoholic fatty liver disease (NAFLD) patients without any treatment	

3)Outcome Measures

Primary Outcome Measure:

① The change of CT ratio of liver/spleen
CT imaging has been used to assess hepatic steatosis and has been validated in relation to liver biopsy. The ratio of liver to spleen (L/S ratio) for CT attenuationvalues is an index, with a L/S ratio<1 considered to represent fatty liver. The

② change of CT ratio of liver/spleen will be assessed at different time comparing with the baseline.

Secondary Outcome Measure:

① general indicators
Basic information and symptoms will be assessed at different time comparing with the baseline
[Time Frame: 3 months, 6months]

② biochemical indicators

Liver function will be assessed at different time comparing with the baseline

[Time Frame: 3 months, 6months]

③ Fibroscan E value

Fibroscan E value is indicators for evaluating liver fibrosis. Changes will be assessed at different time comparing with the baseline

[Time Frame: 3 months, 6months]

④ Changes of gut microbiota

Alpha and Beta diversity of GI microbiota by High-throughput sequencing on baseline

line and 3 months,6months after treatment.

[Time Frame: 3 months, 6months]