Study on Effect of Intestinal Microbiota Transplantation in Chronic Hepatitis B

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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:

• Written informed consent/assent as appropriate

• 18 to 65 years of age

• No alcohol consumption or alcohol consumption <140g per week in men, and <70g per ween in women

• Been diagnosed with chronic hepatitis B

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 injuty(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

• Participating in other clinical trials.

Recuit 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 Combined with Antiviral Therapy 60 chronic hepatitis B patients ongoing antiviral theraoy will be recruited for the sutdy, which involved a 6 times intestinal microbiota transplant and the time interval is generally 2 weeks. Interventions: Procedure: Intestinal Microbiota	intestinal microbiota transplant Participants in Exprerimental group take 6 times IMT with 2-week intervals. Drug: Antiviral Agents All participants continue present antiviral therapy over 12 months.

Transplantation Procedure: antiviral therapy	
Antiviral Agents 60 chronic hepatitis B patients ongoing antiviral theraoy will be recruited for the sutdy, which involved 12 months antiviral therapy. Interventions: Procedure: antiviral therapy	Drug: Antiviral Agents All participants continue present antiviral therapy over 12 months.

3)Outcome Measures

Primary Outcome Measure:

① Decrease of serum hepatitis B virus surface antigen(HBsAg) levels and hepatitis B virus e antigen(HBeAg) levels

Serum hepatitis B virus surface antigen(HBsAg) levels is measured in IU/mL and hepatitis B virus e antigen(HBeAg) levesl is measured in S/CO.

[Time Frame: 1 month, 3 months, 6months]

② Appearance of serum anti-hepatiits B virus surface antigen(anti-HBs) and anti-hepatiits B virus e antigen(anti-HBe)

Appearance of serum anti-hepatiits B virus surface antigen(anti-HBs) and anti-hepatiits B virus e antigen(anti-HBe) suggest the ability of body to resistant HBV.

[Time Frame: 1 month, 3 months, 6months]

Secondary Outcome Measure:

③ Relief of gastrointestinal symptoms

The onset and duration of gastrointestinal symptoms will be assessed by “Evaluation Score Table of Gastrointestinal Symptoms”.

[Time Frame: 1 month, 3 months, 6months]

④ Changes of gut microbiota

Alpha and Beta diversity of GI microbiota by High-throughput sequencing (16S

rRNA) on baseline line and1 month, 3 months, 6months after treatment

[Time Frame: 1 month, 3 months, 6months]