Informed Consent Form

Project name: The effect and mechanism of gene variation on neonatal hyperbilirubinemia

Leading unit: The Sixth Affiliated Hospital, Sun Yat-sen University

Project leader: Hu Hao

Department: Pediatrics

Research period: September 1, 2023 to December 31, 2024

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Application for exemption of informed consent

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Project leader: Hu Hao

Dear Ms / Sir:

We will carry out a study on the the effect and mechanism of gene variation on neonatal hyperbilirubinemia, and invite you to participate in the study. This study has been approved by the Ethics Committee of The Sixth Affiliated Hospital, Sun Yat-sen University.

Please read this informed consent form as carefully as possible before you decide whether to participate in the study. It helps you understand the study and why it was conducted, the process and duration of the study, and the benefits, risks, and discomforts that may result from participating in the study. If you wish, you can also discuss it with your relatives and friends, or ask your doctor for an explanation to help you make a decision. If you are participating in other studies, please inform the researchers.

1. Purpose of the study

Neonatal hyperbilirubinemia, also known as neonatal jaundice, is the most common clinical manifestation of newborns. It has many causes and is difficult to diagnose. Genetic factors are one of the common causes of metabolic-related jaundice. According to statistics, about 60 % to 80 % of newborns can have varying degrees of jaundice, and severe cases can cause a series of body damage, including nerve, hearing, cardiovascular and kidney function, and even cause death. Genetic factors play an important role in the metabolism of bilirubin. Hyperbilirubinemia is mainly caused by bilirubin metabolism or circulatory disorders. It can be clinically manifested as high unconjugated bilirubinemia and hyperconjugated bilirubinemia. The application of genetic testing in this type of disease can improve the early diagnosis of the disease. Genetic testing of children without jaundice or hospitalized jaundice can obtain the proportion of genetic factors and their genotypes in children with jaundice, so as to continuously improve the efficiency of disease diagnosis. However, previous studies have focused on the role of one or two specific genes in patients with

hyperbilirubinemia, and there is no literature report on the study of genetic polymorphism and clinical manifestation polymorphism of jaundice in large data population.

Objective of the experiment:

This study intends to collect heel peripheral blood samples from 2000 newborns [including 500 non-significant (no phototherapy) hyperbilirubinemia newborns, 500 significant (phototherapy) hyperbilirubinemia newborns, 500 severe hyperbilirubinemia newborns and 500 extremely severe hyperbilirubinemia newborns]. The gene capture sequencing technology of common hereditary jaundice genes in newborns containing 24 genes was used to detect the clinical data of these 2000 newborns, and the transcutaneous jaundice instrument (YSJ-20) was used to monitor the daily jaundice at home. According to the results of gene detection and jaundice clinical data analysis of 2000 children, the relationship between common hereditary jaundice pathogenic genes and neonatal jaundice was studied. According to previous studies, neonatal jaundice was found to be closely related to genetic diseases such as Gilbert syndrome, G6 PD deficiency and sodium taurocholic acid co-transfer peptide deficiency. This study will analyze the carrying rate of 24 gene mutations closely related to jaundice in children with neonatal jaundice, to understand whether there is a difference in the carrying rate of pathogenic genes in different degrees of jaundice, and to explore whether there is a difference in the degree of jaundice carrying multiple and single jaundice pathogenic genes. To analyze the correlation between gene polymorphism and clinical manifestations (phenotypic polymorphism) of neonatal hyperbilirubinemia.

1. study process

If you agree to your child 's participation in this study, we will number each subject and establish a medical record.

1. In the course of the study, we need to collect some of your child specimens, which will be sampled by professionals for your children. In this study, 3 drops of peripheral blood were collected from your child 's heel for high-throughput sequencing to detect 24 common neonatal hereditary jaundice genes. Your sample is only used for clinical

research.

2. During the follow-up, you need to measure the jaundice value of your child 's forehead, chest and inner thigh every day, and the use of percutaneous jaundice instrument (YSJ-20) will be guided by professionals.

3. Study risks and discomforts

For your child, all information will be confidential. Your child 's sample collection will be done in strict accordance with the aseptic requirements, and there may be some very small risks associated with the collection of specimens, including transient pain, local bruising, or extremely rare needle infections. If skin cyanosis occurs, we will use magnesium sulfate or hirudoid external application to reduce swelling and remove blood stasis; if needle infection occurs, we will use iodophor disinfection and mupirocin ointment to control infection.

4. Subject responsibilities

As a family member of the subject, you have the following responsibilities: to provide the real situation of the subject 's medical history and current physical condition ; tell the research doctor any discomfort that occurred during the study ; tell the research doctor whether he has recently participated in other studies, or is currently involved in other studies.

5. volunteer

You can choose to disagree with your child 's participation in this study, or at any time notify the researcher to withdraw from the study. Your child 's data will not be included in the study results, and any medical treatment and rights of your child will not be affected.

If your child needs other treatment, or you do not comply with the study plan, or there is a study-related injury or any other reason, the research physician may terminate your child 's participation in the study.

6. privacy protection

If you decide to enroll your child in this study, your child 's participation in the trial and personal data during the trial are confidential. Your child 's blood sample will be identified by the study number rather than the name. Information that identifies your

child will not be disclosed to members outside the research team unless you have permission to do so. All research centers and members are required to keep your child 's identity confidential. Your child 's files will be kept in a locked filing cabinet for researchers to access only. In order to ensure that the study is carried out in accordance with the provisions, members of the government management department or the ethics review committee can consult your child 's information in the research unit as required. When the results of this study are published, no personal information about your child will be disclosed.

The information related to this study and the informed consent form have been reviewed by the ethics review committee of this research institution. If there is any violation of the study protocol during the trial, you can directly complain to the Hospital Ethics Committee. Tel: 020-38379764, E-mail: zslyllb@ mail.sysu.edu.cn

If you volunteer to participate in this study, you need to sign an informed consent form to prove that you have understood the information of the study and agree that your child (the guardian) participates in the study.

You can always understand the information and research progress related to this study. If you have questions related to this study, or if your child has any discomfort and injury during the study, or if you have questions about the rights and interests of the participants in this study, you can contact Hao (researcher) through 020-38777850 (telephone number).

Subject Statement

I have read this informed consent form carefully, I have had the opportunity to ask questions and all questions have been answered. I understand that participation in this study is voluntary, I can choose not to participate in this study, or at any time notify the researcher to withdraw without discrimination or retaliation, any of my medical treatment and rights will not be affected. If I need another diagnosis / treatment, or if I do not comply with the trial plan, or for other reasonable reasons, the researcher may terminate my continued participation in this clinical study. I voluntarily agreed to participate in the clinical study, and I will receive a signed original ' informed consent ' (including personal reading material and informed signature page).

Signature of subject：　　date：

Contact number：

Signature of legal representative [if applicable]：

Relationship with subjects：

Contact number：

date：

Statement by researchers

I have accurately informed the subjects of the content of the informed consent form and answered the questions of the subjects. The subjects volunteered to participate in this clinical study.

Researchers signature：　　date：

Contact number：