PARTICIPANT INFORMATION SHEET (PIS)

TITLE: Evaluation of cystinosis by estimation of leukocyte cystine

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Aims and Purpose of Study

Your child is suffering from renal tubular acidosis in which kidney are unable to remove excess acid from blood. Without treatment, renal tubular acidosis can affect growth and cause kidney stones, fatigue, muscle weakness, and other symptoms. Over time, untreated acidosis can lead to long-term problems like bone disease, kidney disease, and kidney failure.Fortunately, such complications are rare, since most cases can be effectively treated with medicines. There are two type of renal tubular acidosis: distal and proximal.

The most common causeof proximal renal tubular acidosis in children is cystinosis. Cystinosis is a rare disease, causing accumulation of anprotein called cystine within the lysosomes of the body. Lysosomes are a compartment in the cell that breaks down materials such as protein, including cystine. In patients with cystinosis cystine is not allowed to leave the lysosomes causing accumulate within the cell. This accumulation will eventually form into crystals within the cell and start to affect various organs such as kidney, eyes, muscle, pancreas and brain. Damage to the kidneys is most important. In this disease kidneys are not able to concentrate the urine and allows important electrolytes such as sodium, potassium, phosphorus, and bicarbonate to be leaked into the urine. This type of renal tubular acidosis that happen in cystinosis is called Fanconi syndrome.

Cystinosis, like other causes of renal tubular acidosis in children, is a genetic disease and can be easily diagnosed by a genetic test. A genetic test result can take time to come back usually 4 weeks. Another method that can be used for diagnosis is measurement of white blood cell (leucocyte) cystine level. This is a blood test that allows us to measure the amount of cystine accumulating within the cell. This method is quicker but is usually not available widely.

It is important to diagnose cystinosis early becausea specific treatment is available (cysteamine) that decreases the amount of cystine in the lysosomes. Cysteamine is very important as it reduces progression towards kidney failure. While the patient is taking cyteamine, leucocyte cystine level should be checked every 3-4 months. To prevent damage to the child's organs, the level of leucocyte cystine should be kept below 1.0. the amount of cysteamine that is needed depends on these levels.

The aim of the current study is tomeasurewhite blood cell (leucocyte) cystine level in your child's blood so that we can diagnose cystinosis. In addition, genetic test for cystinosis will also be done. This study shall help us to set-up leucocyte cystine assay in the institute and also eventually for patients in our country, that will enable early diagnosis and timely management of patients with cystinosis.

Procedure

Your child who has renal tubular acidosis is invited to join thestudy to estimate leucocyte cystine. It is planned to include about 50such children in this study. With your approval, your physician will note information related to your child's symptoms, treatment and investigations. Further, 8-10 ml (about two teaspoons) blood sample shall be obtained from your child. This will be used for estimating leucocyte cystine levels and for genetic testing for cystinosis. Other

standard management for tubular acidosis shall continue. Follow up visits shall be every three to six for a total of one year. If your child has begun treatment with cysteamine, then at 3 months ad 1-year a same blood sample will be taken to estimate leukocyte cystine. This will tell us whether the dose of medicine is adequate. Your child's sample shall not be used for any study without your or the Ethics Committee's approval.

Expected duration of the subject participation

For purpose of this study, your child is expected to participate in the study for aperiod of one year. During and after this period your child shall be followed up throughthe outpatient clinic as are other children with this condition.

The benefits to be expected from the research to the subject or to others

You are supposed to know about the benefits by allowing yourchild to participate in this study. If elevated leucocyte cystine is detected, treatment can be started early and progression of further kidney injury can be significantly decreased. In case geneticvariations are detected, it will have implications for future pregnancies since this is a genetic disease.

Any risk to the subject associated with the study

No untoward risk to the patient is expected through participation in the study.The treatment of your child's condition shall follow standard guidelines. Collection of small amount of blood (8-10 ml, around twotea spoon full)may cause slight pain and discomfort to the child. However, blood sampling will be done during routine investigations; no extra needle pricks will be done. All aseptic precautions will be followedduring blood sampling. Disposable needles and syringes will be used.

Maintenance of confidentiality of records

The medical records of the patient shall be kept confidential and accessed only by the treating physician or, if necessary, by the Ethics Committee of the All India Institute of Medical Sciences.Your child will not be identified by name anywhere inthe results, discussion or publication.

Cost: All investigations that are being done as a part of the research, including leucocyte cystine level and genetic test, will be done free of cost for you.

Provision of free treatment for research related injuryand compensation for disability or death resulting from such injury

For any complications arising from the primary illness, the child shall receivestandard treatment at the AIIMS. AIIMS does not have any financial liability towardsproviding free treatment for nephrotic syndrome or any attendant complications, duringthis study. Compensation for lost wages (for parents), or discomfort for hospital visits shall notbe provided.

Freedom of individual to participate and to withdraw from research at any timewithout penal or loss of benefits to which the subject would otherwise be entitled

You are free to participate in and with draw from this study at any time you sodesire. This will in no way affect the ongoing treatment of your child at the Institute.

Name and telephone members or individuals to be contacted in case of any questions

In case of any concerns related to your child's treatment, you should contact:

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