The University of Texas Southwestern Medical Center

Title of Research: A Pilot Feasibility Trial of Prenatal and Early Postnatal Fluoxetine Treatment for Intellectual Impairments of Down Syndrome

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Why is this study being done?
This study is being done to see if fluoxetine can improve brain development, intellectual functioning, and behavior of children with Down Syndrome (DS) when given prenatally and postnatally during the first 2 years of life. Below is a summary of information that supports testing of fluoxetine in DS.

1) Normal brain development is disrupted as early as the middle of the second trimester of pregnancy in unborn children with DS, which results in marked disturbances in brain size, shape, and function by birth.
2) Treatments that target brain development prenatally, therefore, may offer a timely opportunity to improve intellectual functioning in DS.
3) Strains of mice have been developed that have the extra copy of Down syndrome genes (like humans with DS). These "DS mice" provide an animal model to test for drugs that could potentially improve brain development in humans with DS.
4) Medications have been recently identified that improve the disturbed processes of brain development/function in DS mice.
5) Fluoxetine, which is an antidepressant marketed as "Prozac," has been the most extensively evaluated, with 7 of 8 studies showing improvements in brain development and function in DS mice.
6) The largest beneficial brain effects with fluoxetine have occurred when treating DS mice early in development. In the only study that treated DS mice prenatally, fluoxetine completely normalized the brain development (leading to normal brain size and number of brain cells) and behavior of DS mice.
7) Much is known about the safety and health of unborn children exposed to fluoxetine prenatally in pregnant mothers with depression and anxiety, where fluoxetine has generally been found safe; although some potentially very serious side effects may occur uncommonly or rarely.

This study is being done to see if the positive results of preclinical studies of fluoxetine in DS translate into positive effects in children with DS.

Fluoxetine has been approved by the U. S. Federal Food and Drug Administration (FDA) for the treatment of other conditions. This is the first study to test fluoxetine in humans with DS. About 21 people will take part in this study at UT Southwestern.

What is involved in the study?
If the researchers believe a pregnant woman and her unborn child meet the study criteria, they will be assigned randomly to receive either fluoxetine or placebo. Study participants will have a 2 in 3 chance of receiving fluoxetine or placebo.

During the prenatal study period, participants will take their assigned medication orally. After her child is born, the mother will stop taking the oral tablet of her assigned medication and her child will start a liquid solution of the medication to be taken orally. After birth, the fluoxetine dose will be adjusted as needed.

Prenatal Study Period
During pregnancy, participants will visit the UT Southwestern Medical Center Obstetrics Clinic monthly. Dr. Robyn Horsager-Boehrer, an obstetrician with expertise in maternal-fetal medicine, will oversee these visits.

Postnatal Study Period
Children born to study participants will be seen for clinical care by Dr. Mary Carlin, the Director of the Children's Medical Center Down Syndrome Clinic. Each child will be evaluated at 3 weeks after birth, 3 months old, 6 months old, and then every three months for 2 years.

The lab tests, EEG tests, MRI procedures, and developmental assessments in this study are designed for research.

What happens with study medication at the end of the study?
At the end of this visit, participants will be told which medication they and their child have been receiving throughout the prenatal and postnatal study periods. If a mother and her child were assigned to fluoxetine, Dr. Carol Tamminga or Dr. Jennifer Giampaolo will discuss whether the mother wants to discontinue the medication or continue taking it in clinical care with a doctor outside of the study.

What are the possible benefits of this study?
We hope that information gained from this research will lead to better treatments that improve developmental abilities in children with Down syndrome.