Dear Families,

After a long while, our team is reaching out with an update regarding a study your child participated in. The purpose of the study was to find out whether two antidepressant medications (Sertraline or Zoloft and Fluoxetine or Prozac) interfered with height growth. Some kids were not taking any medications. We would like to share some updates about this work.

Why did we think about carrying out the study?

Some research studies have shown that certain antidepressants, like Fluoxetine, may interfere with height growth. However, the available findings were limited and not all studies reached the same conclusions. Work from our own lab had shown that perhaps Fluoxetine is more likely to affect height compared to Sertraline.

What did our study try to do?

The study your child participated in set out to compare these two medications and see if markers of growth in the blood were also affected. Based on our earlier work, we suspected that children undergoing puberty would be at highest risk for showing a reduction in growth, if they start taking certain antidepressants. As such, we focused on enrolling kids going through their growth spurt. We initially planned to recruit participants before they started the antidepressant medication. However, this proved difficult, made worse by the COVID pandemic. So, we allowed in kids as long as they had started Fluoxetine or Sertraline within a month. Each child was to be followed for up to 6 months, with visits to the lab at month 0, 2, and 6. At each visit, they underwent a physical exam and a blood draw. The child and the parent also completed questionnaires and met with Dr. Calarge.

Who enrolled in the study?

We had a total of 101 kids in the study, with 39 taking Fluoxetine, 27 taking Sertraline, and 36 not taking either. They were about 12.5 years old, with 70% being girls. They were all undergoing puberty, because of how we designed the study. At the first intake visit, their height and body mass index were normal. Body mass index or <u>BMI</u> is a measure commonly used to determine if someone has excessive weight, with higher values indicating more weight for height.

What did we find?

We found that the higher the dose of the antidepressant, the less a child grew in height but the more their BMI increased. Over the course of 6 months, unmedicated children grew about 1.1 inches and their BMI increased by 0.4 point. In contrast, children taking the equivalent of 40mg of Fluoxetine or 100mg of Sertraline grew by only about 0.6 inches but their BMI increased by 1.4 points. The expected changes in height and BMI would be smaller or non-existent at lower doses or for shorter periods of treatment. Unlike what we had anticipated, the two medications were not different in their effects on height or BMI. We also found that the higher the antidepressant dose, the lower the level of a marker of growth in the blood. The marker is called Insulin Growth Factor 1 (IGF-1). It goes up during puberty, in parallel with the growth spurt.

What questions remain to be answered?

- 1- Medications for depression are sometimes taken for only short period of time. We do not know if stopping the treatment allows the height growth to catch up. We know this process may happen with medications other than antidepressants, like ADHD or ADD medications.
- 2- We do not know if adult height is affected. ADHD or ADD medications are known to affect height growth on the relatively short term, yet adult height is minimally affected, if at all.

How can I learn more about the study findings?

A scientific paper describing all the results has been accepted for publication in the Journal of Clinical Psychopharmacology. We still do not have a link to include in this newsletter, but you can use any web browser (like Safari or Google) to search for the following title: "Fluoxetine and Sertraline Inhibit Height Growth and Growth Hormone Signaling During Puberty." When the paper is out, your web search will find it.

How are we planning to take this research forward?

We used findings from this study to seek additional funding from the Federal Government (the National Institutes of Health or NIH) and are gearing up to start a new study where we compare several antidepressants with each other and with no medications. There are three main differences between the new study and the one your child completed:

- 1- The duration of follow-up is 2 years, instead of 6 months, to allow us to capture any effect of these medications on height growth over a longer period.
- 2- We will get an x-ray of the hand, over time, to see if these medications are affecting bone age. Bone age helps us understand how much height growth each child still has.
- 3- The number of children enrolled will be larger.

We are also pursuing more funding to help determine if adult height is affected in individuals treated with antidepressant medications.

Should antidepressants not be used because they can affect height?

The short answer is "absolutely not". All medications have side effects. The responsibility of a prescriber is to weigh the pluses and minuses of using a medication, no matter what the medication is. Antidepressants are used to treat depression and anxiety, among other conditions. These conditions can be very serious, causing a lot of problems. Leaving them untreated may be dangerous. The best approach is to always discuss medical decisions with your treating clinician.

What if you have more questions?

If questions arise based on this newsletter, please contact us at 832-824-5002. However, please know that we may not be able to release information about your child specifically, beyond what we have already shared with you.

In closing, our team would like to sincerely thank you for taking part in the study. Without your time and commitment, this advance in medical knowledge would not have been possible.