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Cystic Fibrosis Research News

Title:

Lens-related ocular changes in fetal rats following in-utero exposure to elexacaftor-tezacaftor-ivacaftor

Lay Title:

Changes in eye development in baby rats exposed to ETI when in the womb

Authors:

Yimin Zhu[1], Mengliang Wu[2], Danni Li[1], Mark Habgood[1], Holly R. Chinnery[2], Elena K. Schneider-Futschik[1]

Affiliations:

[1] Department of Biochemistry and Pharmacology, School of Biomedical Sciences, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, Parkville, VIC 3010, Australia

[2] Department of Optometry and Vision Sciences, University of Melbourne, Victoria, Australia

What was your research question?

We aimed to investigate whether the use of elexacaftor-tezacaftor-ivacaftor (ETI) during pregnancy could impact eye development in newborns by using a rat model.

Why is this important?

ETI has greatly improved the lives of people with CF. However, we do not fully understand whether it is safe for women to continue taking ETI during pregnancy. Cataracts occur when the normally clear lens in the eye becomes cloudy and have been reported in some babies born to mothers who took ETI during pregnancy. Ivacaftor, a key part of ETI, has also been linked to cataracts in young children with CF and in animal studies. Therefore, understanding the effects of ETI on eye development is essential for pregnant women to make safe treatment decisions.

What did you do?

We treated pregnant rats with either a sham treatment (control group) or ETI drugs at doses comparable to those is currently used in humans. The drug was administered daily throughout the mid to late stages of pregnancy (equivalent to the last trimester of human pregnancy). After birth, we examined the eyes of the newborn rats using imaging techniques that use light to capture images of the eye structure. We then analysed eye tissues that were stained with

dye to identify changes in the cells. Key eye parameters, including lens cavities, were measured and compared between the rat groups exposed to ETI and the control rat groups to assess the impact of ETI on eye development in the womb.

What did you find?

We found no evidence of major structural changes that could indicate the formation of cataracts in the eyes of rat pups exposed to ETI during pregnancy. However, the images showed an increase in lens thickness in those exposed to ETI compared to the control group, but other key measures of eye development remained unchanged in the eyes of the both groups. Interestingly, lens cavities were observed in both groups. Although the images did not show differences in cavity sizes in the two groups, the tissue analysis showed that that ETI-exposed pups had larger individual lens cavity sizes.

What does this mean and reasons for caution?

These findings suggest that ETI does not cause major defects in eye development in pups exposed to ETI during late pregnancy. However, the increase in lens thickness and lens cavities in those exposed to ETI suggest that ETI could potentially alter lens-related development. The reasons for our observations are unclear, and further studies are needed to fully understand how ETI may impact lens development. Additionally, our study focused only on late-stage pregnancy exposure while most CF mothers are exposed to treatment from early pregnancy.

What's next?

In future studies, we will give ETI from the start of pregnancy to understand whether the increased lens thickness and lens cavities seen in ETI-exposed pups in this study will be more pronounced with longer/earlier exposure. This will help to ensure its safety for babies' eye development when used during pregnancy.

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