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Cystic Fibrosis Research News

Title:
A case report of CFTR modulator administration via carrier mother to treat meconium ileus in a F508del homozygous fetus

Lay Title:
Maternal Trikafta use during pregnancy and breastfeeding improved outcomes for a baby with CF

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What was your research question?
We report a fetus (baby) who was known to have CF before birth. Ultrasound showed a bowel blockage called meconium ileus, which often requires surgery and is associated with worse CF outcomes. The pregnant mother, who did not have CF, asked about taking Trikafta during pregnancy to help her baby.

Why is this important?
Modulators used to treat CF are associated with improved lung function, nutritional status and quality of life. Studies of modulator safety are happening in younger age groups with interest in preventing or reversing CF complications. Some CF complications begin before birth. Not much is known about risks and benefits of *in utero* (before birth) modulator exposure for babies with CF. *In utero* exposure can be achieved by the pregnant mother taking the medication. In this case, the fetus had meconium ileus, which often results in long hospitalization, surgery, pain and suffering for the baby, and added stress for the family.

What did you do?
The patient/family, CF team, obstetricians, and neonatologists discussed potential risks, benefits and unknowns of treatment to both maternal and fetal health. Meconium ileus usually does not resolve by itself and the potential to avoid surgery was heavily weighted. Following shared decision-making, we treated the pregnant mother with Trikafta beginning

at 32 weeks gestation. We followed health of the mother and baby before and after birth. After birth, the mother continued taking Trikafta while breastfeeding the baby.

What did you find?

The fetal meconium ileus resolved on ultrasound 27 days after the mother started Trikafta. The baby was born in good health and went home without surgery on the 2nd day of life. The baby, known to be F508del homozygous, had normal fecal elastase, consistent with pancreatic sufficiency. Sweat chloride was consistent with CF but much lower than expected for F508del homozygous infants. Liver laboratory testing was normal for both the mother and the baby. The mother tolerated Trikafta and continued treatment while breastfeeding. The baby continues to thrive and be pancreatic sufficient.

What does this mean and reasons for caution?

Resolution of meconium ileus *in utero* and pancreatic sufficiency in a F508del homozygous infant suggest benefit of Trikafta exposure before birth and during breastfeeding. There are ethical considerations including incomplete safety data for treating an unaffected mother and a developing baby, generally unknown effectiveness of treatment before birth and via breastmilk, and cost of treatment. Additionally, under current FDA approvals, the baby is not eligible to start modulator therapy until age 2, resulting in a potential treatment gap.

What's next?

This case highlights the possibility of reversing or preventing complications of CF with very early modulator treatment. More data about modulator safety and effectiveness during pregnancy, lactation and infancy are needed to guide informed treatment decisions in the future.

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