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Cystic Fibrosis Research News

Title:

CFTR modulator therapy via carrier mother to treat meconium ileus in a F508del homozygous fetus: insights from an unsuccessful case

Lay Title:

Treating cystic fibrosis before birth: What we learned from an unsuccessful case

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What was your research question?

Can a cystic fibrosis (CF) medicine, called elexacaftor/tezacaftor/ivacaftor (ETI), help treat a baby with CF before birth if given to the mother? We wanted to see if the medicine could reach the baby through the placenta and help with a blocked intestine (meconium ileus) before birth.

Why is this important?

Some babies with CF develop a blocked intestine (meconium ileus) before birth, which often requires surgery after delivery. ETI has helped people with CF, and a few reports suggested it

might also help unborn babies when given to the mother. If successful, this treatment could reduce the need for surgery and improve the baby's health. However, we don't yet know the best time to give the medicine, the right dose, or if enough of it reaches the baby. More research is needed to see if this could be a safe and effective way to treat CF before birth.

What did you do?

A pregnant woman whose baby was diagnosed with CF and meconium ileus was given ETI at 27 weeks of pregnancy. Doctors hoped the medicine would pass from the mother to the baby through the placenta and help clear the blockage. The baby's intestines were checked regularly with ultrasound. After birth, doctors tested the baby's blood and the mother's breast milk to see how much of the medicine had reached the baby. They then compared this case to other cases where ETI had worked, looking for possible reasons why the treatment didn't succeed this time.

What did you find?

Even though the mother took ETI, the baby was still born with a blocked intestine and needed emergency surgery. Tests showed very little of the medicine had reached the baby through the placenta or breast milk. In previous cases where ETI helped, the treatment started later (30-32 weeks), so starting earlier in this case (27 weeks) didn't seem to make a difference. Other factors, like the mother's weight or differences in how the medicine is passed to the baby, may have played a role. This suggests that ETI might not always work before birth, and more research is needed.

What does this mean and reasons for caution?

This study shows that ETI might not always help treat CF before birth. While some babies in other cases improved, it's unclear if the medicine made a difference or if their condition would have improved naturally. The amount of medicine that reached the baby was low, meaning ETI may not easily pass through the placenta. Also, each pregnancy is different, and factors like the mother's weight may affect how much medicine the baby gets. More research is needed before this treatment can be recommended. We need to better understand the right timing, dosage, and how the medicine reaches the baby.

What's next?

More cases need to be studied to understand if ETI can help babies with CF before birth. Future research should focus on how medicine actually reaches the baby, whether the dose

should be adjusted, and when to start treatment. Clear guidelines are needed before this can be a routine treatment.

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