Sigma Theta Tau International's 29th International Nursing Research Congress

Two Unexpected Pregnancies Attributable to Cystic Fibrosis Gene-Specific Drug Therapy: A Case Study

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Purpose: The purpose of this case study is to describe the experiences of an adult woman with cystic fibrosis who became pregnant twice while on IVA/LUMA after several years of trying to conceive unsuccessfully. Cystic fibrosis (CF) is no longer a disease of childhood. This autosomal recessive disease affects 70,000 people worldwide, and over 10 million people carry the defective gene (CF Foundation, 2017). The median predicted survival age for individuals with CF has climbed steadily since it was first described in the 1930s (CFF, 2014). With advances in genetic testing, drug discovery, and comprehensive clinical care, people with CF are living well into their fourth decade of life (CFF, 2017) and engaging in all developmental milestones, including parenthood. With the recent FDA approval of two gene-specific drug therapies, ivacaftor and combination ivacaftor-lumacaftor (IVA/LUMA) (CFF, n.d.), implications for fertility and reproductive health are largely unexplored.

Methods: Two audio-taped, semi-structured interviews were conducted with the woman with CF. Interviews were transcribed and reviewed for accuracy prior to analysis. Narrative analysis was conducted to identify key experiences and gaps in clinical care and research.

Results: Ana (pseudonym) is a 29-year-old woman with CF who was diagnosed with CF at four months old. She has homozygous DF508del, the most common CF genetic variant that affects approximately half of those with CF (CFF, 2017). She has multiple CF-related co-morbidities including: pancreatic insufficiency, recurrent sinusitis, and gastrointestinal obstructions. She began IVA/LUMA therapy in August 2015 shortly after FDA approval, and two weeks later found out that she was pregnant after trying unsuccessfully to conceive with her husband for two years. The only change in her regimen was IVA/LUMA. She reported that she always had thick cervical mucus, a classic clinical presentation of CF in women, which blocks sperm transport (McArdle, 2011). Within two weeks of IVA/LUMA, her pulmonary function tests increased by six percentage points, her energy levels rose, and her sinus congestion improved. When she happily notified her CF care team about her pregnancy, which she directly linked to IVA/LUMA, she was counseled to discontinue the drug because it has no specific safety profile available for pregnant women. She advocated to stay on the drug because of her improved quality of life. Her son was born slightly premature at 34 weeks gestation, and stayed in the neonatal intensive care for three weeks due to breathing difficulties. He is now a healthy toddler who is developmentally on track for his age. When he was seven months old, Ana found out that she was pregnant again. She was on IVA/LUMA throughout the first pregnancy and afterwards. She reported that with IVA/LUMA, her mucus, both from her lungs and cervix, were thinner. She continued to be on IVA/LUMA with her second pregnancy that has been largely smooth and uneventful. At the time of this abstract development, Ana is 38 weeks gestation and awaiting the arrival of another son.

Conclusion: There are a few anecdotal reports of women becoming pregnant on IVA/LUMA; however, there are no official numbers of these pregnancies being tracked by the CF Foundation's Data Registry. Post-marketing research needs to be conducted in order to develop the safety profiles of these targeted therapeutics in order to facilitate an informed dialogue between CF providers and patients regarding the appropriate initiation and use of these drugs in women of childbearing age. CF providers must engage patients in regular and sensitive discussions related to reproductive and sexual health, including the potential for improved fertility due to CF drugs like IVA/LUMA, and the need for effective contraception if they do not wish to become pregnant. In a seminal study of women with CF, only 33% understood how CF affects fertility, and 84% reported not using any form of contraception while sexually active (Korzeniewska et al., 2009). Moreover, in another study of women with CF who became pregnant, 22% of these pregnancies were terminated due to either unplanned pregnancy or deteriorating health status (Roe et al., 2015). The vast implications for fertility, sexual, and reproductive health in this vulnerable group of

women in the era of personalized medicine must be investigated. Pregnancy and motherhood are especially complex events for women with CF who have heavy treatment burdens related to their own health maintenance. An unexpected pregnancy has the potential to result in catastrophic outcomes for the woman with CF and/or her fetus. Therefore, it is critical to monitor any pregnancies that occur after initiation of CF targeted therapeutics like IVA/LUMA, and additional research is warranted to ensure their safe use in pregnant women.

Title:
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Keywords:
cystic fibrosis, pregnancy and targeted therapeutics

References:
Cystic Fibrosis Foundation (CFF). (2017). *About cystic fibrosis*. Retrieved from https://www.cff.org/What-is-CF/About-Cystic-Fibrosis/

Cystic Fibrosis Foundation (CFF). (2014). *Cystic Fibrosis Foundation patient registry: 2012 annual data report.* Bethesda, MD: Cystic Fibrosis Foundation.

Cystic Fibrosis Foundation (CFF). (n.d.). *CFTR modulator therapies.* Retrieved from https://www.cff.org/Life-With-CF/Treatments-and-Therapies/CFTR-Modulator-Therapies/

Korzeniewska, A., Grzelewski, T., Jerzynska, J., Majak, P., Soloniewicz, A., Stelmach, W., & Stelmach, I. (2009). Sexual and reproductive health knowledge in cystic fibrosis female patients and their parents. *Journal of Sexual Medicine, 6*(3)*,* 770-776. doi:10.1111/j.1743-6109.2008.01049.x

McArdle, J. R. (2011). Pregnancy in cystic fibrosis. *Clinics in Chest Medicine, 32*(1), 111-120. doi:10.1016/j.ccm.2010.10.005.

Roe, A. H., Traxler, S. A., Hadjiliadis, D., & Schreiber C. A. (2015, May). *Contraceptive needs and preferences in a cohort of women with cystic fibrosis.* American Congress of Obstetricians and Gynecologists, Annual Clinical and Scientific Meeting. San Francisco, CA.

Abstract Summary:
A woman with cystic fibrosis became pregnant twice on ivacaftor/lumacaftor after years of trying to conceive unsuccessfully. Safety profiles for this drug have not been established for pregnant women. Implications for research, practice, and education related to CF drug therapy are vast for this vulnerable group.

Content Outline:
I. Purpose

A. Describe experiences of adult woman with CF who became pregnant twice while on IVA/LUMA after years of trying to conceive unsuccessfully

B. Cystic fibrosis (CF) no longer a disease of childhood

C. Median predicted survival age into the fourth decade of life

D. CF gene-specific drug therapies (e.g., ivacaftor and combination ivacaftor/lumacaftor [IVA/LUMA]) – implications for fertility and reproductive health unexplore

II. Methods

A. Two audio-taped, semi-structured interviews with woman with CF

B. Transcribed and reviewed for errors

C. Narrative analysis to identify experiences and gaps in clinical care and research

III. Results

A. Ana (pseudonym) – age 29, homozygous DF508del genetic variant

B. Became pregnant two weeks after starting IVA/LUMA, after two unsuccessful years of trying to conceive with her husband

C. Only change in her medical regimen was IVA/LUMA

D. Directly attributed her pregnancy to IVA/LUMA

E. CF care team recommended discontinuation of IVA/LUMA because of lack of safety data on drug – Ana stayed on drug throughout pregnancy and afterwards

F. Son delivered 6 weeks early due to premature labor, currently a healthy toddler

G. While son was 7 months old, Ana became pregnant again

H. Second pregnancy uneventful - currently at 38 weeks gestation, awaiting arrival of second son

IV. Conclusion

A. Anecdotal reports of pregnancy on CF gene-specific drugs, not tracked by CF Foundation Data Registry

B. Post-marketing research on these drugs needs to be conducted to establish safety profiles and facilitate informed dialogue between CF providers and patients regarding appropriate use

C. Discussions on fertility, reproductive, and sexual health must be done regularly and sensitively as part of comprehensive clinical care

D. Unplanned pregnancies in women with CF has potential for catastrophic results for the woman and/or fetus

E. Additional research on safety of personalized medicine in CF is warranted

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Professional Experience: 2014-Present, Assistant Professor, University of Alabama at Birmingham School of Nursing; Birmingham, AL 2014-2014, Lecturer, University of Central Florida College of Nursing; Orlando, FL 2008-2014, Instructor, University of Central Florida College of Nursing; Orlando, FL 2004-2008, Visiting Instructor, University of Central Florida College of Nursing; Orlando, FL Record of scholarship and excellence as evidenced by multiple presentations, publications, honors and awards (i.e., presented twice at the International Nursing Research Congress of Sigma Theta Tau, and selected as the Nurse of the Year by the March of Dimes Foundation, Central Florida Chapter) Leadership skills as evidenced by my leadership roles in national and local professional organizations, and within my academic institution

Author Summary: Dr. Sigrid Ladores is a PhD-prepared pediatric nurse practitioner and nurse educator with 20 years of experience. She is an emerging leader in the area of reproductive health issues in cystic fibrosis. She has several peer-reviewed publications, and presented her research in international, national, regional, and state conferences.