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Community Health / Policy

Abstract Title

A New Start Before Birth: Prenatal Decision-Making for Life-Threatening Hypophosphatasia in the Era of In-Utero Therapy

Authors

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Background

Hypophosphatasia (HPP) is a rare monogenic condition caused by pathogenic variants in the ALPL gene. Variants in this gene result in decreased activity of tissue non-specific alkaline phosphatase, which is crucial for bone and tooth formation beginning in-utero. Life-threatening HPP (LT-HPP) is a severe form of HPP that can be detected by prenatal ultrasound and confirmatory molecular testing. Historically, LT-HPP has been associated with high mortality in the first year of life. Bone-targeted enzyme-replacement therapy (ERT) begun after birth has significantly reduced mortality in LT-HPP. However, surviving children still face challenges with growth, dentition, seizures, craniosynostosis, and physical disability. In-utero enzyme-replacement therapy (IU-ERT) is an emerging treatment approach being considered for LT-HPP. It involves the administration of alkaline phosphatase directly into the fetal circulation, under ultrasound guidance beginning at approximately 22 weeks' gestation, to take advantage of the unique window of fetal bone development and mineralization.

Objective

The aim of this research study is to explore the perceived benefits, barriers, and attitudes of IU-ERT among families with prior experience with LT-HPP, and couples at risk of having a child with LT- HPP.

Methods

We propose to conduct an exploratory qualitative study using semi-structured interviews with individuals

and families with prior experience with LT-HPP, and couples at risk of having a child with LT-HPP. Interview data will be analyzed to identify key themes related to perceived benefits and risks of IU-ERT and its potential impact on prenatal decision-making.

Results

Data collection and analysis are ongoing.

Conclusion

Anticipated Impact: This novel research study will examine perceptions of in-utero treatment for a rare and debilitating genetic condition. The results of this study will directly inform genetic counselling practices for the HPP community across Canada. Additionally, the study's outcomes could support clinical decision-making for patients with life-threatening HPP by clarifying treatment considerations and expected outcomes.