Investigating the response to anesthesia in a zebrafish model of CHARGE syndrome

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Presenter Information

Jessica is a third year medical student at Dalhousie University and is working on a project investigating adverse events following anesthesia administration in individuals with CHARGE syndrome using a zebrafish animal model. Her research is supervised by Dr Kim Blake and Dr Jason Berman and is conducted in the Berman lab which has a zebrafish model of CHARGE syndrome. Jessica completed a Master's in Science before entering medical school, during which she conducted research in cardiovascular pharmacology. She is interested in both the clinical and research aspects of CHARGE syndrome, and has very much enjoyed modelling what has been seen clinically in the lab in hopes of furthering the understanding of the mechanisms of CHARGE.

Presentation Abstract

Background: Individuals with CHARGE syndrome experience adverse events during and following anesthesia. We examined the response to anesthesia in a zebrafish model of CHARGE (loss of chd7 expression) to investigate causative factors. We used zebrafish retaining chd7 expression as control.

Results: There was a difference in baseline heart rates between the CHARGE model of zebrafish (loss of expression) and the controls. Exposure of the CHARGE and control zebrafish to anesthesia revealed behavioural differences. We measured time to anesthesia and the CHARGE zebrafish took longer to become anesthetized and had a higher respiratory rate during the anesthetic recovery period compared with the control fish. Videos will demonstrate differences between CHARGE and control zebrafish.

Conclusion: We were able to demonstrate differences in response to anesthesia between CHARGE compared with control zebrafish. CHARGE zebrafish took longer to become anesthetized, which is consistent with what is seen clinically. During recovery, the CHARGE zebrafish had higher respiratory rates. Future work will investigate survival outcomes of CHARGE versus control zebrafish.

Learning Objectives

- Individuals will have insight into the utility of our zebrafish model of CHARGE syndrome.
- To understand the anesthesia complications in CHARGE syndrome that have been observed clinically and the response that we see to anesthetic in our zebrafish model of CHARGE.
- To help professionals and families advocate for a better understanding of complications of undergoing anesthesia.

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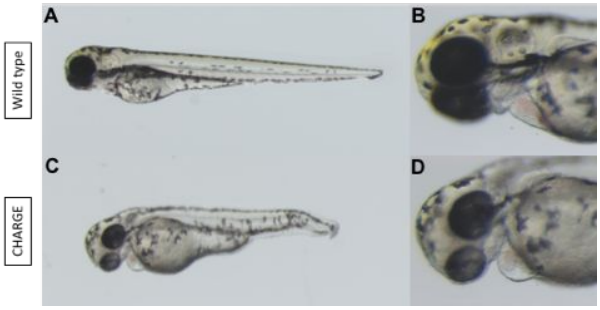
Individuals with CHARGE syndrome experience adverse events during and following anesthesia. In order to investigate further, we examined the response to anesthesia in a zebrafish model of CHARGE syndrome that our lab created.

Zebrafish are a good model organism for lab-based studies of human disease as they develop quickly, are less expensive to house than other model organisms, and share many of the same genes and molecular pathways with humans.

We made our CHARGE model by creating a zebrafish that does not express the gene chd7 (found to be mutated in CHARGE syndrome). We have previously shown features of CHARGE syndrome in our fish, such as gastrointestinal dysmotility, heart defects and abnormal spinal curvature[1-3]. We will show videos of the CHARGE zebrafish model. We decided to see if our CHARGE fish could be used to study response to anesthesia in CHARGE syndrome.



Loss of *chd7* expression in the zebrafish results in a CHARGE syndrome phenotype.
Representative images of control (A, B) and our *chd7* CHARGE zebrafish (C, D).

In order to study anesthesia in the zebrafish we recorded heart rates, opercular beats (similar to respiratory rates in humans) and the time it took the fish to become anesthetized (lose response to touch) and recover from anesthesia (regain response to touch). We compared the CHARGE fish to control fish, in whom expression of chd7 was intact.

We discovered the following:

1) **CHARGE fish required more time in anesthetic to become anesthetized.**
2) **The respiratory rates of CHARGE fish did not drop as low as other fish when anesthetized, and they were higher during the recovery period from the anesthetic.**
3) **CHARGE fish had lower heart rates when exposed to anesthesia when compared to other fish.**

We were able to demonstrate differences in response to anesthesia between CHARGE compared with control zebrafish. CHARGE zebrafish took longer to become anesthetized, which is consistent with what is seen clinically. During recovery, the CHARGE zebrafish had higher respiratory rates. Our zebrafish model has provided new insights into the symptoms experienced by CHARGE patients during anesthesia. CHARGE syndrome is associated with a number of issues believed to be related to vagal nerve dysfunction such as trouble swallowing, acid reflux and constipation. The vagus nerve is also involved in the autonomic nervous system, which plays a role in modulating heart and respiratory rates. It is possible that vagal nerve dysfunction contributes to the differences in heart and respiratory rates when the CHARGE fish are exposed to anesthesia.

References

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