Developmental Effects of Lamotrigine on Zebrafish Embryos

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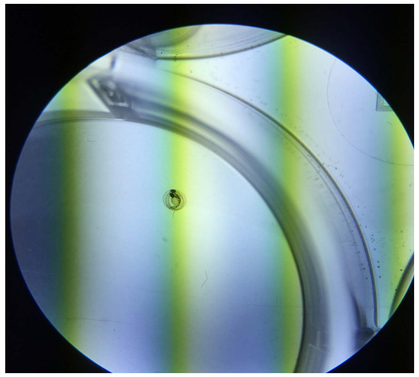
Abstract

Our experiment tested the effects of Lamotrigine, a drug used in the treatment of neurological disorders, on the development of zebrafish embryos. Correlations between the drug and development observed in the embryos can help us predict the influence that Lamotrigine might have on the development of a human fetus. Currently, there have been no conclusive studies confirming whether the drug has an effect on human fetal development. Our experiment will add to the research that already exists and educate pregnant women taking Lamotrigine about possible deformities in their babys' development. Our data suggests that higher doses of Lamotrigine actually accelerates the development of the zebrafish embryos.



Control (0% Concentration Lamotrigine Solution)

Introduction

Lamotrigine is a medication that is typically used for treating conditions such as Epilepsy, Bipolar Disorder and other neurological disorders. Lamotrigine works by enhancing the actions of GABA, an inhibitory neurotransmitter, which can then reduce pain transmission signals through nerves. Some common side effects of taking this drug are blurred vision, skin rashes and poor coordination. Although Lamotrigine has been scientifically demonstrated to have antiepileptic effects in patients with seizure disorders, recent studies have found that the use of this drug during pregnancy may also have adverse developmental effects on the fetus. One study done on rat offspring whose mother took Lamotrigine while pregnant revealed that the newborns experienced deformities of teeth and genitals and expressed hyperactive behavior (Sathiya 2014). Another case studying rat hippocampal slices found that exposure to Lamotrigine decreased the output of basket cells, which can negatively impact cerebral function and memory (Yu-Yin 2016). Lamotrigine has been proven to have prevent seizures in patients; however, there have not been many previous studies on developmental effects observed in offspring whose mothers have been exposed to the drug. Through this experiment we intended to find whether this medication delays the development of zebrafish embryos. We hypothesized that the embryos in the Lamotrigine solutions would experience deformities and possibly slower development than those in the control solution.

Materials & Methods

Materials

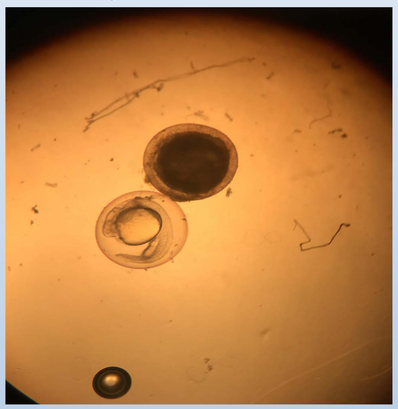
One 150 mg Lamotrigine pill, one stirring rod, 4 beakers, 2 Falcon dishes, 1L of 200µg/L Instant Ocean solution, a 1L flask, pipettes, an incubator

Method

1. 1L of Instant Ocean solution was poured into a 1L flask and the 150 mg tablet of Lamotrigine was dissolved completely into the solution
2. 4 clean beakers were used to make the solutions of regular dose (20 ml of Lamotrigine solution and 80 ml of instant ocean solution), half dose (10 ml of Lamotrigine solution and 80 ml of instant ocean), double dose (40 ml of Lamotrigine solution and 80 ml of instant ocean solution), and our control (with no medication at all and 80 ml of instant ocean).
3. 3 ml of each type of solution (2 trials for each) was loaded into the wells of the falcon dishes
4. 5 embryos were placed into each well
5. A microscope was utilized to examine each embryo and decide which stage of development it was in at the time, according to the reference book we had been given. The stage of each embryo, the number of dead embryos, and the number of embryos that had hatched was recorded in the Day One data table
6. The Falcon dishes were placed in the incubator at 28℃
7. Steps 5 and 6 were repeated for Day Two and Day Three
8. The Standard Error of the Mean was found for the average stages of each dose on each day in order to add correct error bars to each graph

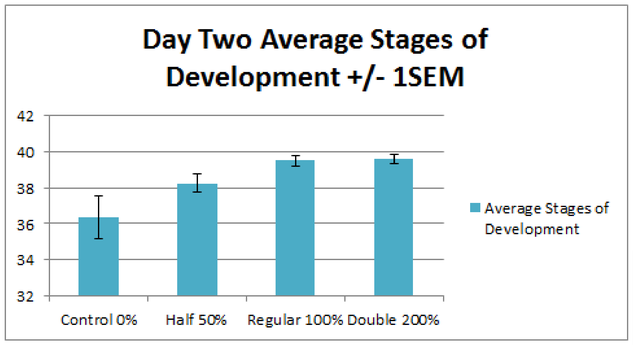
50% Concentration Lamotrigine Solution

100% Concentration Lamotrigine Solution



Results

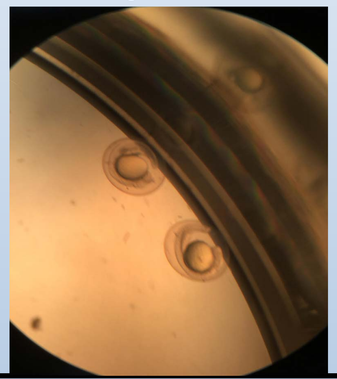
Zebrafish embryos were exposed to different doses of Lamotrigine to determine whether the drug had any developmental effects. The embryos were randomly placed in one of four different wells: a control with no Lamotrigine, a "half dose"(50% concentration), a "regular dose"(100% concentration), and a "double dose"(200% concentration). From this experiment we observed that higher concentrations of Lamotrigine actually accelerated the development of the zebrafish embryos overtime.



Discussion

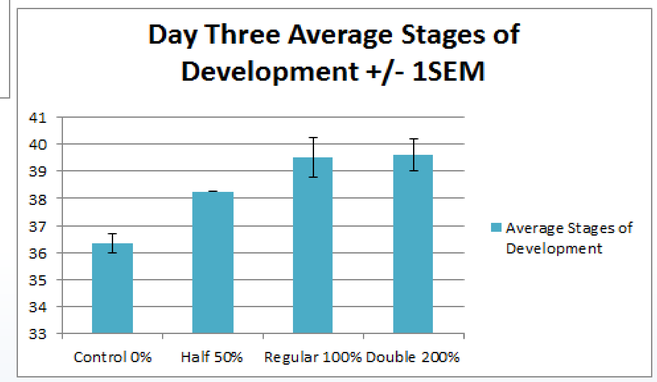
Our data failed to support our hypothesis because, overall, the higer doses of Lamotrigine resulted in higher stages of embryo development than the lower concentrations. Our data demonstrated that the medication actually accelerated the development of the zebrafish embryos overtime. One error that we encountered in this experiment was a sudden reduction in sample size that was not related to effects of the drug we were testing. On day two of observations, petri dish 2 was knocked over, killing most of the embryos and forcing the survivors to be transferred into dish 1. This sample size reduction may have influenced our overall data, as the embryos in dish 2 were either killed or relocated. From the findings, however, we can conclude with 68% confidence that Lamotrigine significantly accelerates the development of zebrafish embryos. Therefore, it is likely that the medication would have no stunting effects on the fetuses of pregnant women. However, accelerated development may cause other issues with the pregnancy. Anyone considering this or any medication to treat neurological disorders should consult a physician first, especially women who are or plan to become pregnant.

200% Concentration Lamotrigine Solution



Data Analysis

On the day one graph, there is no significant difference between the development of embryos in the Control, Regular, and Double doses. However, found that the embryos in the Half Dose of Lamotrigine had significantly higher average stages of development than those in the Control and Double Dose solutions. On the Day Two graph, there is no significant difference between the average development of embryos in the Regular and Double doses. The average development of the Half dose embryos was also significantly higer than that of the Control embryos. The average development of embryos in the Regular and Double Dose are significantly higher than those of both the Control and Half doses. On the Day Three graph, once again there was no significant difference between the average development of the embryos in the Regular and Double doses. Like with the Day Two graph, we found that the Half Dose embryos had a significantly higher average development than those in the Control, and the Regular and Double Dose had significantly higher average developments than both of the lower concentrations.



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