

Do safer seizure medication choices during pregnancy result in fewer birth defects?

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In their study “Declining malformation rates with changed antiepileptic drug prescribing: An observational study,” Dr. Tomson and coauthors¹ analyzed 14 years of data from pregnant women with epilepsy. Their goal was to find out how seizure medication choices and pregnancy outcomes have changed over time. The data came from an international pregnancy data registry called EURAP.

What is the EURAP registry and how does it work?

A clinical data registry is a database that records medical information about patients over time to gather knowledge about particular medical conditions. EURAP is an international registry that records data about pregnant women who take seizure medications in Europe, Australia, Asia, and South America.² There is a separate pregnancy registry in the United States and Canada called the North American Antiepileptic Drug Pregnancy Registry.³

The EURAP registry currently includes data from over 25,000 patients in 44 countries since 1999.² Before there were pregnancy registries for women with epilepsy, little was known about the safety of seizure medications during pregnancy. This is because pregnant women cannot go through drug trials. The main goal of EURAP is to learn about risks associated with taking seizure medications during pregnancy, and to record any birth defects that occur.⁴ Doctors encourage pregnant women who have been taking seizure medications since conception to enroll in the registry to help us learn about seizure medication safety in pregnancy.

What have we learned from the EURAP registry in previous research?

Multiple studies about seizure medication safety during pregnancy have been published since the EURAP registry began. A recent large study including data from 7,355 pregnancies was published by Dr. Tomson and colleagues⁴ in 2018. The study included women who were taking 1 of the 8 common seizure medications.

The authors found that the seizure medication associated with the highest rate of birth defects was valproate (10.3% of pregnancies) (table). Other medications with higher rates of birth defects included phenobarbital, phenytoin, and carbamazepine. Medications with lower rates of birth defects included oxcarbazepine, levetiracetam, and lamotrigine. Risks of birth defects for oxcarbazepine, levetiracetam, and lamotrigine were between 2% and 3%, which is similar to the rate of birth defects in women who do not take seizure medications.

What were the main findings of this study?

The goals of the current study were to determine whether doctors have changed their seizure medication choices in pregnant women based on new safety data published previously from the EURAP registry. They also asked whether those medication choices have resulted in a decreased rate of birth defects in babies born to these women.

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Table EURAP results: Rate of birth defects in babies born to women taking seizure medications during pregnancy, by medication type

Medication taken during pregnancy	Percentage of pregnancies with birth defects
Valproate	10.3
Phenobarbital	6.5
Phenytoin	6.4
Carbamazepine	5.5
Topiramate	3.9
Oxcarbazepine	3.0
Lamotrigine	2.9
Levetiracetam	2.8

Study of EURAP data from 2000 to 2013 showed that there was a decline in use of higher risk medications and an increase in lower risk medications levetiracetam and lamotrigine over time. The rate of birth defects decreased over time, from 6.0% in 2000–2005 to 4.4% in 2010–2013. This is a 27% decrease (figure). Birth defect rates for individual medications stayed about the same, although birth defect rates for all medications combined went down. This reflects the shift to use of lower risk medications. The rate of

convulsive (generalized tonic-clonic) seizures reported during pregnancy did not change.¹

What does this mean for pregnant women with epilepsy?

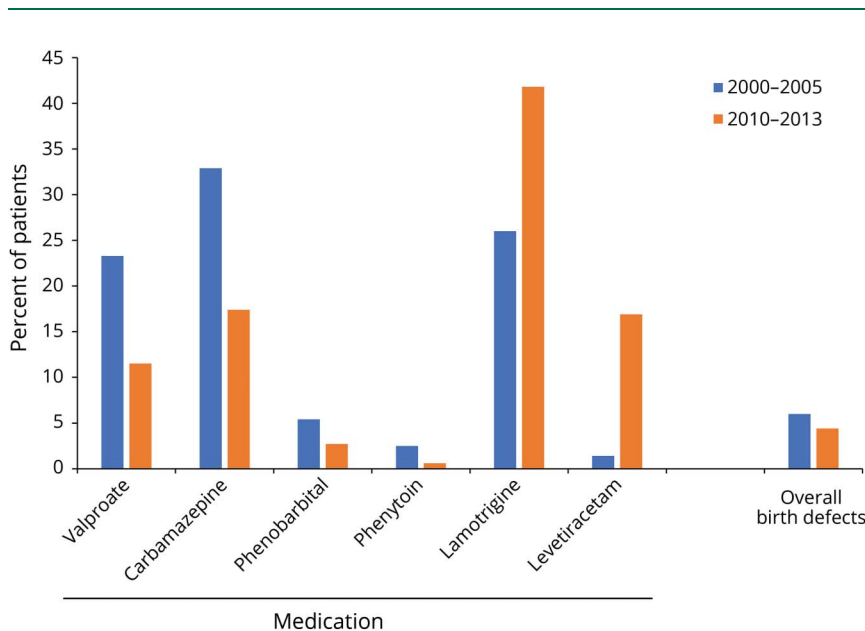
This study found a change in prescribing patterns. Doctors are prescribing fewer higher risk seizure medications for pregnant women and more lower risk seizure medications. The overall rate of birth defects decreased over time. There was evidence that the reduction in birth defects was related to decreasing use of higher risk medications, particularly valproate. Other reasons such as improving prenatal care did not explain the improvement. The change in medications used during pregnancy did not result in more serious seizures.

These results give doctors and patients more confidence that it is safer to choose levetiracetam and lamotrigine when possible for pregnant women with epilepsy over higher risk seizure medications.

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Figure Medications taken during pregnancy compared to rate of birth defects during 2 time periods (2000–2005 and 2010–2013)



About seizures and epilepsy

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Adapted from Smith DM. Genetic testing: About epilepsy and genetics. Neurology 2019;92:e523–e526; and Karceski S. Pregnancy, antiseizure medications, and seizures: About epilepsy. Neurology 2018;91:e1271–e1274.

What are seizures?

The cells of your brain use chemicals and electrical signals to talk to each other. Most of the time, this electricity is like a room of people talking—there is constant chatter but none of the voices stand out. If a group of cells starts sparking off electricity together in coordination with each other, it is as if they are talking loudly together, making a sound that can be heard above the crowd. The coordinated electrical signals create a sort of electrical storm or surge, which is a seizure. Seizures can look like many different things, depending on how many cells are talking, and where those cells are in the brain.

This is why there are many different types of seizures. Most people have heard of the grand mal type seizure, where a person becomes stiff all over and has shaking movements of the whole body. Other seizures may look similar to this, only involving one half of the body. People may or may not lose consciousness during a seizure. A seizure can be nothing more than a muscle jerk, over in less than a second. It can be a few seconds of staring off. It can vary a great deal from person to person.

What is epilepsy?

People have seizures for different reasons. Some children have seizures when they have a high fever. Some people with diabetes have seizures when their blood sugar gets low. These seizures are provoked, or set off, by something else. It is the fever or the blood sugar that is the problem, not the brain. In epilepsy, there is nothing provoking the seizures. Seizures happen for no reason. In epilepsy, doctors use seizure medications to prevent seizures. In provoked seizures, doctors usually do not use seizure medications.

What causes epilepsy?

There are many different reasons why people can get epilepsy. Sometimes, epilepsy happens after there is an injury to the brain. For example, epilepsy can happen after a concussion, after a stroke, or after a brain infection. Sometimes, doctors can tell the cause of epilepsy by looking at a picture of the brain. However, for many people, no brain injury ever happened, and there is nothing wrong on the picture of their brain. For many of these people, their epilepsy may be genetic, or may be caused by a problem too small to see with a brain scan.

How are seizures treated?

There are many treatments for seizures. Medicines are tried first. If these do not work, a doctor may consider special diets, brain surgery, or devices for the treatment of seizures. The goal is to stop all seizures without causing side effects. In women who are pregnant, or thinking about becoming pregnant, it is especially important to consider safety when choosing medications. There are certain medications that are known to have a higher association with birth defects. Often, in women who are thinking about starting a family, these medications are avoided. When choosing a medication, it is important to have a discussion with your doctor about your life plans: work, exercise, and the desire to start a family. Taking all of these things into consideration, together you will make the best choice of treatments.

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