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<http://www.epilepsyfoundation.org/epilepsyusa/news/Anticonvulsant-Valproic-Acid-Increases-Risk-of-Congenital-Disorders.cfm>

Anticonvulsant Valproic Acid Increases Risk of Congenital Disorders

Results from a new study confirm that taking the anticonvulsant valproic acid in the early stages of pregnancy not only increases the risk of spina bifida, but also of other major congenital malformations. This risk is also higher than that of other anticonvulsants. This should be considered when choosing an anticonvulsant for women who would like to have children, now or in the future, according to researchers of the Pharmacoepidemiology and Pharmacoeconomics department of the University of Groningen and the University of Ulster in an article published in the *New England Journal of Medicine* on June 10 (<http://content.nejm.org/>).

In addition to spina bifida, the study links use of valproic acid in the first trimester to other congenital malformations: atrial septal defect, cleft palate, hypospadias, polydactyly (an extra finger or toe), and craniosynostosis (premature fusion of skull sutures). The risk of spina bifida proved to be 12.7 times higher in the valproic acid group compared to the women not using anticonvulsants.

The researchers are a part of a network for the registration of congenital disorders, the European Surveillance of Congenital Abnormalities (EUROCAT), and they used EUROCAT's antiepileptic-study database in the valproic acid study. The pregnancies described in the database—the largest ever used for such a study—are from registrations of congenital malformations in 14 European countries.

In the period covered by the study, nearly 4 million pregnancies and 100,000 children with a congenital malformation were recorded.

The authors stated that despite the increased risk for several congenital malformations, it is important to recognize that the absolute rates of specific malformations are still relatively low, and a sizeable majority of children are born without defects. It is also important to consider the goal of optimizing seizure control in the individual patient. Therefore, the authors conclude, the decision should be made by the patient and her clinician after consideration of the benefits and risks of various anticonvulsant medications.

In a direct comparison with other anticonvulsants, valproic acid proves to impart a higher risk of all the congenital malformations listed above, except that the risk of craniosynostosis was not significantly increased; however, valproic acid use was associated with a significantly increased risk of ventricular septal defect. Given that it is difficult to switch medication just before pregnancy, as it takes time for the patient to adjust to the new drug, researchers feel that when choosing medication for women who may want to have children in the future, it would be wise to consider the risk of congenital malformations.

Current guidelines from the American Academy of Neurology recommend avoiding valproic acid in pregnant women, if possible, because of the risk for congenital malformations, as well as poor cognitive outcomes.

[Page B. Pennell, M.D.](#), Chair of the Epilepsy Foundation Professional Advisory Board and Director of Research for the Epilepsy Division of the Department of Neurology at Brigham and Women's Hospital, a Harvard Medical School teaching affiliate, in Boston, wrote:

The findings from this study provide key details for consideration when treating adolescent girls and women with epilepsy. The design of this study, from a population-based congenital anomaly registry with a large number of births, identified which specific major congenital malformations were more likely to occur in the offspring of women on valproic acid compared to not only women who were not taking antiepileptic drugs, but also women on other antiepileptic drugs.

The findings allow us to make better-informed decisions when choosing medications in women of all ages, and allow us to provide better counseling to our female population. This study replicates the overall message from other studies, which is: By choosing any anticonvulsant other than valproic acid, you are automatically lowering risks for that pregnancy. This is empowering for both the provider and the women living with epilepsy as they plan for their future.