Viinikainen, Katriina. Epilepsy, female reproductive health and neurodevelopment of the offspring. Series of Reports, No 87, Department of Neurology, University of Kuopio 2007. 85 p.

ISBN 978-951-781-379-2 ISBN 978-951-27-0217-6 (PDF) ISSN 0357-6043

## **ABSTRACT**

One of the most common neurological diseases in women of childbearing age is epilepsy, affecting approximately 0.8 percent of the women. An increased risk for both fetal and maternal complications, has been reported in women with epilepsy due to epilepsy itself, epilepsy related co-morbidities and antiepileptic drugs. Some of the frequent concerns are reproductive problems, pregnancy complications, congenital malformations and developmental problems in the offspring.

The purpose of this study was to evaluate the fertility and reproductive health in women with active epilepsy living in the Kuopio University Hospital area. The study was also extended to evaluate the pregnancy outcome of these women and to the assessment of the cognitive and neurological performance of the children exposed to valproate and carbamazepine monotherapy during pregnancy.

We found no difference between women with epilepsy and control women in their reproductive health and also the overall rate of women having children was the same, if we exclude the infertility caused by a higher proportion of severe co-morbid factors, which differentiate the women with active epilepsy from the general population. We followed the pregnant women throughout the pregnancy with a pre-decided protocol. The course of pregnancy was uncomplicated in the majority of the women with epilepsy. Congenital malformations were observed in 4.8 % of the live-births in women with epilepsy and the rate of small-fordate infants as well as the rate of admissions to a neonatal intensive care unit, were higher in the infants of the women with epilepsy. Women using valproate for epilepsy had a lower intelligence quotient than women using carbamazepine or women without antiepileptic drugs and also their level of education was lower, reflecting perhaps the nature of the epilepsies responding specifically to valproate. Children exposed to valproate had also lower mean intelligence scores, though the difference did not reach statistical significance. They also scored lower values in the neuropsychological tests and had received more educational support than children exposed to carbamazepine or children without drug exposure. In 62 % of the children exposed to valproate, one or more minor dysmorphic features were observed compared to 15% in other children. Children with carbamazepine exposure did not differ from controls.

In conclusion, women with active epilepsy represent a particularly challenging population for neurologists and other health care professionals. However, in our population with the pre-decided protocol used for the follow-up of pregnancies and well controlled epilepsy, the majority of the women with epilepsy have uncomplicated pregnancies. The risk for congenital malformations is nearly two-fold in the offspring of women with epilepsy exposed to antiepileptic drugs compared with the results of the national malformation registry. The cognitive outcome of children exposed to carbamazepine does not differ from controls, which is in line with previous reports. Our findings suggest that valproate may have a negative impact on neurocognitive development of the exposed offspring, though many confounding factors, including the type of epilepsy and level of schooling of the mother, may explain some of this result.

National Library of Medicine Classification: QV 85, WL 385, WQ 210, WQ 240

Medical Subject Headings: Carbamazepine/adverse effects; Epilepsy; Finland; Infant, Newborn; Maternal Exposure; Pregnancy; Pregnancy Complications; Pregnancy Outcome; Pregnant Women; Prenatal Exposure Delayed Effects; Risk; Uterus/drug effects; Valproic Acid/adverse effects

Contact: katriina.paloviita@fimnet.fi