

## The effects of epilepsy medication on women's health and fertility

By Cecilie M. Lander

Women of reproductive age who have epilepsy have a number of specific concerns and issues. The complexity of modern society contributes to these concerns. For instance, a young woman of eighteen with newly diagnosed epilepsy does not want to relinquish any of the 'normal' expectations of her age group. Ideally, she will want to be in control of her life and therefore wants her epilepsy controlled with suitable medication that is at once effective and free of adverse side effects. She wants to have a career of her choice and to be able to drive a car. She wants effective contraception and when ready, safe conception, uneventful pregnancies and healthy children. Is all of this possible?

The answers of course are many and varied according to every woman's specific situation. However, the reality is that the woman with epilepsy will have less chance of achieving all of these goals than her sister who does not have epilepsy. Here is a brief discussion around some of these questions.

### Which antiepileptic drug should be used for a woman of reproductive age?

Firstly, it is necessary to state - and sometimes to re-state - that whenever possible, epilepsy should be controlled as much as possible. Epilepsy remains a very significant problem and a potentially a dangerous one.

Therefore, in every case where active epilepsy occurs, the most appropriate drug for the specific type (syndrome) of epilepsy should be used. Sometimes this is not

possible because of adverse or allergic reactions to that medication, and a second choice has to be used. As a general rule, (and exceptions will occur), valproate and lamotrigine are the drugs of first and second choice for Primary Generalized epilepsies. The dose is the one that controls the epilepsy.

If there is any possibility of an unexpected pregnancy, then it is a reasonable "insurance" to take a the daily requirement of 1mg folic acid as well.

Which antiepileptic drugs interfere with the efficacy of the oral contraceptive pill (OCP)?

Anti epileptic drugs (AEDs) which are hepatic 'enzyme inducers' will enhance the metabolic breakdown of OCPs, and hence increase the risk of unexpected conception. These include phenytoin (Dilantin), carbamazepine (Tegretol), barbiturates (Phenobarb, Prominal, Mysoline) and the newer drug, topiramate (Topamax).

If these AEDs are used, then there should be consideration for a somewhat higher oestrogen containing OCP or an alternative or added contraceptive method.

### Will AEDs affect weight?

While there are reports of many AEDs tending to cause weight gain, valproate (Epilim, Valpro) is probably the most recognized. Topiramate may actually induce weight loss.

### **Does the menstrual cycle affect the seizure pattern?**

Catamenial epilepsy (increased epilepsy around the time of the menstrual period) is a fact for many women. There are two peaks in epilepsy occurrence - one at the time of ovulation and another just before or during the menses. This occurs because of direct hormone effects on epilepsy and the effects of hormones on AEDs.

### **Do AEDs have any effect on bone health?**

The older enzyme inducing AEDs such as phenytoin and carbamazepine seem to have a tendency in a few women to enhance osteopenia. However there is also a report that valproate in children could potentially change bone metabolism. Little comment can be made about the new AEDs in this regard. In general however, the potential gain from these drugs over a long period of time has outweighed the longer term bone risks. It is, in individual patient, impossible to tell if there will be significant long term bone changes as a result of AED use.

### **Will epilepsy and AEDs affect fertility and reproduction?**

Most women with epilepsy will have little problem conceiving and producing a healthy child. However there are some increased risks.

Statistics show that women with epilepsy have fewer marriages and somewhat fewer children than their non-epileptic sisters. Clearly there are many reasons for this, many of which are social.

However, active, uncontrolled epilepsy that causes tonic-clonic generalized seizures is associated with an increased risk of foetal loss- miscarriage and stillbirths. This is very high (30 - 50% foetal loss) if status epilepticus occurs.

There have been a number of reports that suggest that valproate is associated with an increased risk of polycystic ovaries but other reports indicate that this condition of polycystic ovaries may be found in up to 1 in 5 women with epilepsy regardless of medication. For the most part, just having polycystic ovaries (PCO) is not necessarily

associated with any symptoms at all.

There is a more advanced condition known as the polycystic ovary syndrome (PCOS) which is polycystic ovaries in conjunction with infertility, obesity, a tendency to diabetes and hyperlipidemia. Because of infertility and potential metabolic abnormalities, this is of greater concern. While this condition also occurs in the wider female population, it may be marginally increased in epileptic populations and is probably enhanced, at least in some women, by valproate.

It has been found that up to 30% of menstrual cycles in epileptic women are anovulatory and this is observed more often in partial (locational) epilepsies than in primary generalized ones. Clearly this is a potential cause of infertility.

The possible effect of AEDs on the development of the child is an important subject. It is not possible to answer all the questions on this issue here. In brief, all AED's approximately double the 'normal population' risks of malformations in the child. However, it is also very important that the mother's epilepsy be controlled.

To discover the exact risk of each drug or drug combination on the developing baby is a difficult task. However the Australian Pregnancy Register (1 800 069 722) has been established for women with epilepsy who are pregnant to help answer exactly this question. This Register will collaborate with other Pregnancy Registers in Europe and North America.

Folic acid and vitamin B supplements are regarded as very important prior to and during early pregnancy. Vitamin K supplements are routinely given to the new born baby and often to the mother late in pregnancy.

Usually, women with epilepsy can safely breast feed their babies.

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