PREGNANCY OUTCOMES IN CLINICAL PRACTICE

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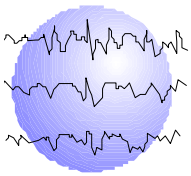

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RATIONALE

Young women with epilepsy are eager to enjoy full productive lives including bearing children. There has long been a fear regarding the effect of the pregnancy on seizures and the effect of epilepsy and its treatment on the fetus/infant. Over the last five years numerous registries have been developed within the USA and globally to evaluate the effects of antiepileptic drugs (AEDs) on pregnancy outcomes (North American Registry, EURAP, Australian and UK Registries). We evaluated our pregnancy outcomes before and after approval of the new AEDs.

METHODS

Questionnaires were sent to women in our practice who were pregnant between 1995 and the present. Questions and information were given in written format and by telephone communication. Women who wished to participate signed consents and returned the information in pre-stamped return packets. Also included was a self-addressed, prepaid envelope to receive a complete report from the authors when the project is finished. Questions regarding all pregnancies were asked including age, folate use, AED use, seizures during pregnancy, delivery type, any birth/delivery complications, fetal loss, ultrasound results, and developmental status of the child with each pregnancy. For this study, old AEDs were defined as those approved prior to 1990 and new AEDs were those approved after 1990.

RESULTS

101 questionnaires were sent out and 40% have been returned. Twenty-Seven patients reported information on 39 pregnancies, which included one pregnancy with twins. 76% of the mothers were on monotherapy and 24% were on polytherapy. Sixteen babies (48%) were exposed to old AEDs in monotherapy and 13 babies (34%) were exposed to the newer AEDs. Nine (23%) babies were exposed to two antiepileptic drugs. (fig 1) Two were exposed to phenobarbital (PB) and valproic acid (VPA), three to carbamazepine (CBZ) and lamotrigine (LTG), two to VPA and levetiracetam (LEV), one to CBZ and PB, and one to LEV and LTG. Mothers taking monotherapy antiepileptic drugs included 10 (34%) on CBZ, 5 (17%) on LTG, 4 (14%) on LEV, 3 (10%) on PB, 2 (1%) on phenytoin (PHT), 2 (7%) on oxcarbazepine (OXC), 1 (3%) on VPA, 1 (3%) on gabapentin (GBP), and 1 (3%) on topiramate (TPM). (fig 2) No mothers were on more than two AED's during these pregnancies.

There were thirty-five live births in 34 pregnancies. There were five unsuccessful pregnancies; one tubal pregnancy (CBZ and PB), one trisomy pregnancy (CBZ), one extra set of chromosomes (LEV), one still birth (CBZ) and one abruptio placenta (LTG). (fig 4) Four of the five unsuccessful pregnancies were exposed to folic acid.

There were no major congenital abnormalities. There were 8 (23%) abnormal outcomes in the live birth group defined as delayed development in speech or motor milestones requiring therapy and special programming. Five of the developmentally delayed were exposed to the older AEDs in monotherapy (3 CBZ, 1 PB, 1 VPA). Two were exposed to new AEDs (both to LTG), and one on polytherapy with LTG and LEV. Seven of the eight abnormalities occurred despite folate supplementation. (fig 5)

Three of the eight mothers whose babies had developmental delay had seizures during pregnancy. One mother had three complex partial seizures and one generalized tonic-clonic seizure in the first trimester. One had two complex partial seizures in the second trimester and one had other seizures (auras, simple partial or myoclonic) in each of the trimesters. (fig 5)

Sixteen women had seizures at some time during pregnancy: 6 had a single GTC, one had 2, 7 had CP's. 3 had auras or SP's. There were no cases of status. Folate was supplemented in 86.7% of live births at doses of 1-4mg/day.(fig7)

Eight mothers had illnesses or some other problems during pregnancy and had normal babies. Of the eight mothers, two had pre-term labor (one with gestational diabetes), one had elevated liver function tests, one had hypertension and diabetes, two had upper respiratory infections, one had severe reflux and vomiting, and one was just pregnant at the time she had surgery for grid placement to record seizures, and a second surgery for grid removal and focal surgery. She also did not have OB care until her sixth month of pregnancy.

Conclusion

Women with epilepsy can and do have successful pregnancies. They have some chance of fetal loss. More subtle developmental delays and need for early special services and therapy for the child may be more prevalent than previously recognized with both old and new AEDs. Awareness of this potential concern may direct a choice in AEDs, as well as allow the parents to advocate for the child earlier.

This is a first report of an ongoing study of pregnancy and its outcomes for women with epilepsy in our clinic.

Figure 1

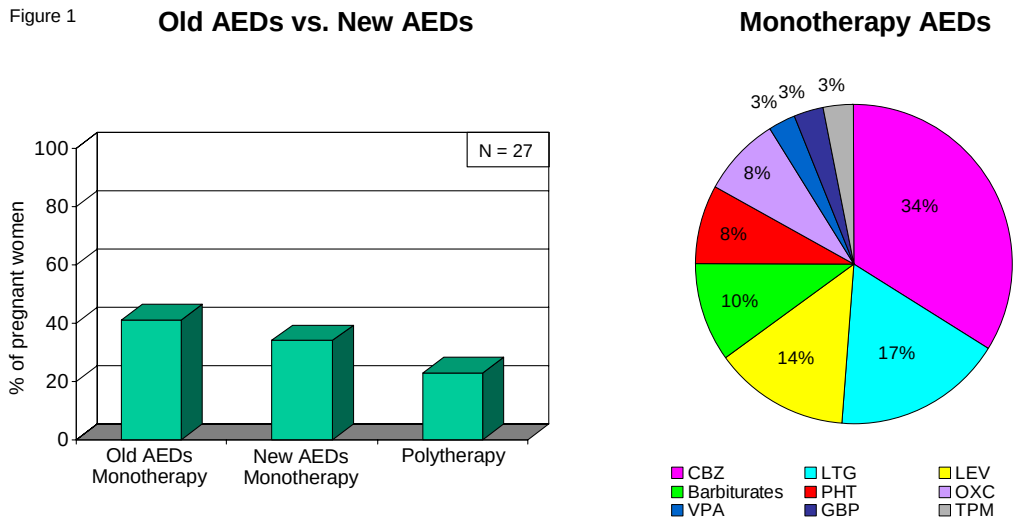


Figure 3

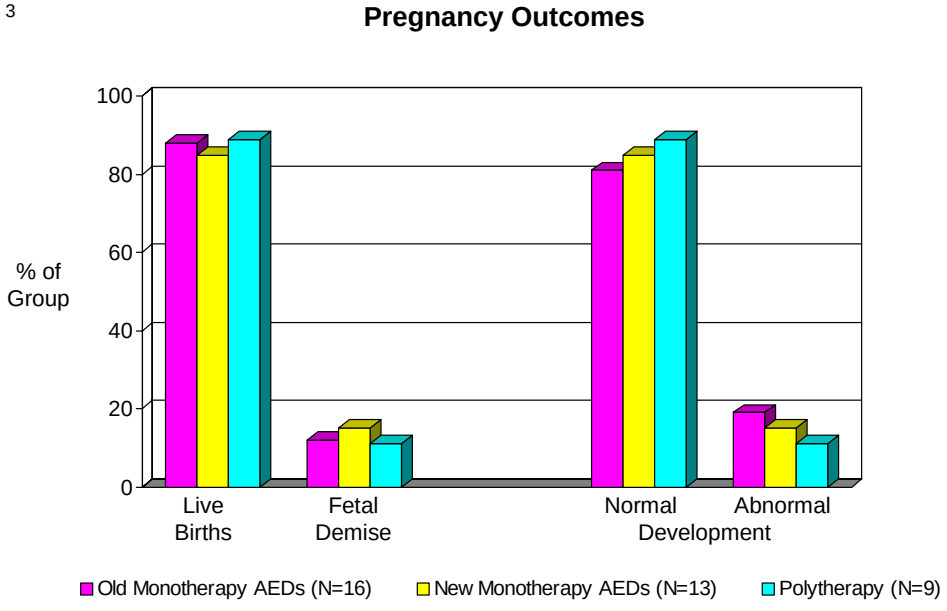


Figure 4

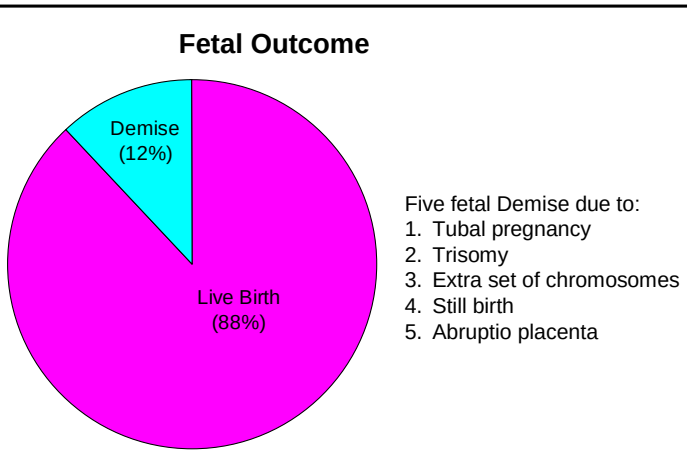
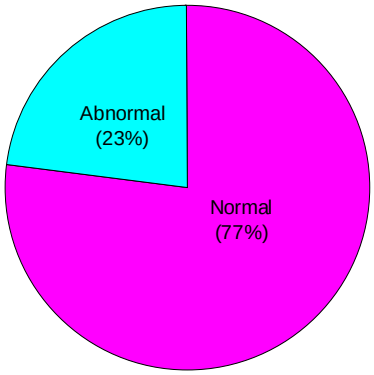


Figure 5



Abnormalities		Folic Acid	Seizures	AED	Outcome
1		Yes	3 complex partial and 1 generalized tonic-clonic in 1st trimester	LTG	Mild learning disability
2		?	None	PB	Speech Delay
3		Yes	2 complex partial in 3rd Trimester	CBZ	Aspergers syndrome
4	twins	Yes	None	CBZ	Delayed motor and speech, hypotonicity (both parents mentally retarded)
5	twins				
6		Yes	Auras and/or simple partial seizures throughout pregnancy	SVP	Speech and motor delay Benign hypotonicity
7		Yes	None	LEV & LTG	Unknown
8		Yes	None	LTG	Delayed motor and speech

Figure 6

Seizure Frequency Pre Pregnancy

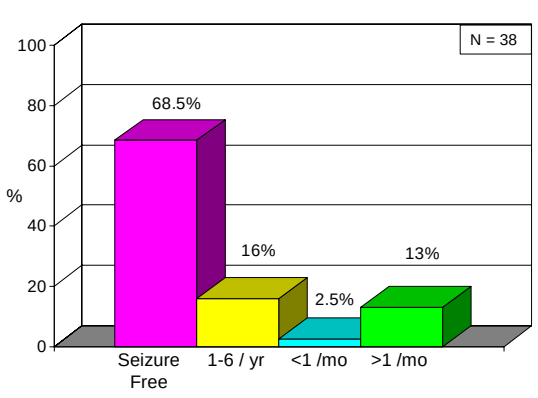
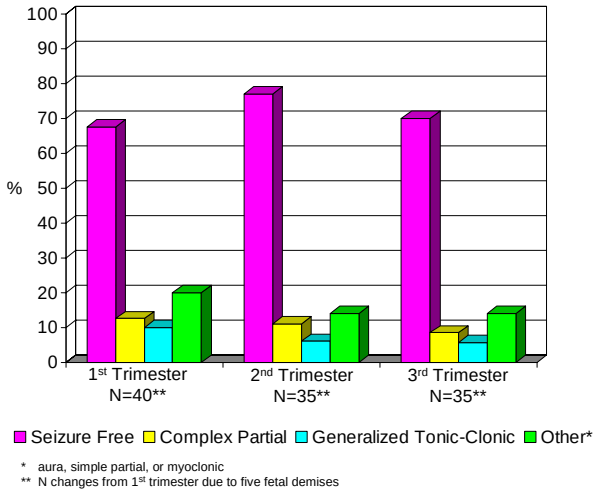


Figure 7

Seizure Frequency During Pregnancy



* aura, simple partial, or myoclonic

** N changes from 1st trimester due to five fetal demises