# Choosing AEDs in Special Situations

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#### WOMEN

#### Case scenario\_1

A 28 years old woman with 7 years-history of automotor seizures. She is taking Phenytoin 300 mg a day and has been seizure free for 1 year. She proposes a plan of having a child.

### Prepartum Counseling

#### **AT DIAGNOSIS**

- Careful history taking
- Perform evaluation before AED: EEG, MRI, VEEG (PNES)
- Start the AED (appropriate and with low risk of TRG)
- Discuss available data on TRG risk (AED chosen)
- Discuss risks of seizures and AED noncompliance (in general & pregnancy)
- Start folic acid 0.4-4 mg/d along
- Ensure adequate contraception

2016	Rate of MCM	CBZ	GBP	LTG	LEV	OXC	РВ	РНТ	TPM	VPA
n Special Situation_Epilepsy Course for Resident	Australian Pregnancy Registry	5.5% (346)	0% (14)	4.6% (307)	2.4% (82)	5.9% (17)	0% (4)	2.4% (41)	2.4% (42)	13.8% (253)
	Danish Registry	-	1.7% (59)	3.7% (1019)	0% (58)	2.8% (393)	-	-	4.6% (108)	-
	International Registry of Antiepileptic Drugs and Pregnancy	5.6% (1402)	-	2.9% (1280)	1.6% (126)	3.3% (184)	7.4% (217)	5.8% (103)	6.8% (73)	9.7% (1010)
	Finland National Birth Registry	2.7% (805)	-	-	-	-	-	-	-	10.7% (263)
	GlaxoSmithKline Lamotrigine Registry	-	-	2.2% (1558)	-	-	-	-	-	-
	North American AED Pregnancy Registry	3.0% (1033)	0.7% (145)	2.0% (1562)	2.4% (450)	2.2% (182)	5.5% (199)	2.9% (416))	4.2% (359)	9.3% (323)
AEDs	Norwegian Medical Birth Registry	2.9% (685)	-	3.4% (833)	1.7% (118)	1.8% (57)	7.4% (27)	-	4.2% (48)	6.3% (333)
hoosing	Swedish Medical Birth Registry	2.7% (1430)	0% (18)	2.9% (1100)	0% (61)	3.7% (27)	14% (7)	6.7% (119))	7.7% (52)	4.7% (619)
wongse K_C	UK/Ireland pregnancy registry	2.6% (1657)	3.2% (32)	2.3% (2098)	0.7% (304)	-	-	3.7% (82)	9% (203)	6.7% (1290)

### Prepartum Counseling

#### **1 YEAR OF PRECONCEPTION**

- Adequate evaluation in uncontrolled cases
- Consider epilepsy surgery in appropriate one
- Consider AED reduction/withdrawal in whom, seizure free for 2-4 years
- + Establish trough AED levels 2 times a year
- + Discuss balance (risks of AEDs & seizures during pregnancy)
- Discuss a need to adjust dose during pregnancy
- Continue folic acid
- + Ensure adequate contraception during AED adjustment



Modified with permission from Tomson T, Battino D, Lancet Neurol.17www.thelancet.com/journals/laneur/article/PIIS1474-4422(12)70103-5/abstract. B 2012 Elsevier Ltd.



Reprinted with permission from Baker G, et al, Neurology.24 <u>www.neurology.org/content/84/4/382.short</u>. B 2014 American Academy of Neurology.

# Prepartum/Pregnancy Counseling

#### **PERI/POSTCONCEPTION**

- Confirm patient is taking folic acid
- Discuss appropriate prenatal screening or genetic counseling
- Targeted anatomic ultrasound at 20 weeks
- Discuss social support, seizure safety in caring for infants, and need to avoid sleep deprivation
- Discuss breast-feeding
- Establish a pregnancy plan
- + Advice to notify doctors on first sign of pregnancy

#### **Obstetrical & Perinatal Outcomes**

- WWE may be at increased risk for obstetric complications e.g., preeclampsia, and postpartum hemorrhage, preterm birth, and IUGR.
- Neither epilepsy nor AED use is usually an indication for a cesarean delivery.

## **Breast Feeding**

- PRM and LEV probably/GBP, LTG, and TPM possibly penetrate into breast milk in potentially clinically important amounts.
- Children exposed to CBZ, LTG, PHT, or VPA in breast had higher IQs and language scores at 6 years of age when compared to those children whose mothers did not breast-feed.



Practice Parameter update: Management issues for women with epilepsy—Focus on pregnancy (an evidence-based review): Vitamin K, folic acid, blood levels, and breastfeeding Report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society

#### Case Scenario\_2

Q 24 years old woman with history of 2 years of partial onset epilepsy, taking CBZ 300 mg/d. She has been free from seizure for 1.5 years. She would like to get advice regarding to family planning.

#### Interactions between AEDs & HC

AEDs	Effect on HC	Affected by HC
Clonazepam, diazepam, ethosuximide, ezogabine, gabapentin, lacosamide, lorazepam, levetiracetam, pregabalin, vigabatrin, zonisamide	None	None
Carbamazepine, clobazam, eslicarbazepine, oxcarbazepine, phenobarbital, phenytoin, primidone, rufinamide	Decrease EE levels Decrease PG levels	Unknown
Topiramate	Decrease EE levels (dose dependent)	Unknown
Perampanel	Decrease PG levels	Unknown
Lamotrigine	Decrease PG levels	Decrease LTG (estrogen HC)
Valproate	None	Decrease VPA (estrogen HC)

### Contraception

- CDC and WHO advise against EIAEDs combined with OCP, the vaginal ring, or the transdermal patch. However DMPA can be safely used while of etonogestrel subdermal implant should be used with additional contraceptions.
- The most reliable form of reversible contraception for any WWE is IUD (pregnancy <1%).</li>



GluAED

AED Monotherapy

No AED

EIAED

InhAED

NEIAED

#### Case Scenario\_3

№ 17 years old teen with history of epilepsy whose seizures increase markedly around her period.



Catamenial epilepsy : a pattern of increased seizures at specific times in the menstrual cycle that are characterized by an increased estrogen-toprogesterone ratio.

Harden CL, Pennell PB, Lancet Neurol.74 www. thelancet.com/journals/laneur/article/PIIS1474-4422(12)70239-9/abstract. B2013 Elsevier Ltd.

# Catamenial Epilepsy

- Management should begin with standard AED therapies. Several adjunctive treatments include acetazolamide, clobazam, clomiphene citrate, GnRH, DMPA (seizure reduction >> 50% in 40-60%).
- Women with the C1 pattern were most likely to be responders, with 21% to 57% of them having a 50% or more seizure reduction (200 mg progesterone lozenges tid for D+14 to +25).



#### ELDERLY



# Epilepsy in Elderly

- Common etiologies include CVA, neurodegenerative diseases (AD), and malignancy.
- 28-55% of elderly patients in the EMU had a nonepileptic etiology identified, and between 1/4-1/2 of these patients were on AEDs for these events.

Ramsay RE,, Neurology 2004. Abubakr A, Epilepsy behav 2005, McBride AE, Epilepsia 2002.

### Status Epilepticus in Elderly

- Acute symptomatic seizures are more common in elderly patients, as is status epilepticus.
- The annual incidence of status epilepticus in patients 60 years or older is nearly twice that of the general population (86 per 100,000).

#### Status Epilepticus in Elderly

 In generalized SE, PB was the most successful initial treatment (71%), followed by LZP (63%), then DZP and PHT (53%), and PHT alone (42%)

For subtle status, PB was the most effective (31%) followed by LZP (14%).15

Treiman DM, Epilepsy Res 2006.

## AEDs Use in Elderly

- Age-related changes including decreases in renal clearance, hepatic blood flow and liver size, decreases in GI absorption, and decreases in serum albumin (>>decreased protein binding), resulting in greater sensitivity to AE of AEDs.
- FBM, GBP, LCM, LTG, LEV, OXC, PGB, TPM, and VGB decreased clearance of > 20% in older adult.

### AEDs & Hepatic interactions

Strong enzyme inducer	Weak to moderate CYP 3A4 enzyme inducers	No significant hepatic enzyme interaction	Hepatic enzyme inducers
Carbamazepine	Oxcarbazepine	Clonazepam	Valproic acid
Phenytoin	Topiramate	Diazepam	Felbamate
Phenobarbital	Felbamate	Gabapentin	Oxacrbazepine
Primidone	Clobazam	Lacosamide	Eslicarbazepine
	Rufinamide	Lamotrighine	
	Eslicarbazepine	Levetiracetam	
		Lorazepam	
		Perampanel	
		Pregabalin	
		Vigabatrin	
		Zonisamide	
		Adapted from Carlson C. An	derson CT. Continuum 2016

### AEDs & Organ Failure



## AEDs Use in Elderly

- A trend for increased tolerability was present for LTG versus CBZ-SR; however, there was also a trend for increased efficacy with CBZ-SR.
- In a 12-month trial, LTG had the highest retention (56%), followed by GBP (49%) and CBZ-IR (36%), with no significant differences in seizure control.



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8 มกราคม 2560 January 2016 วิ่งกินลม ชมพระราชวัง รำลึกความหลังเซาดิน เยือนถื่นสุภาพบุรุษลูกผู้ชาย วิ่งผ่อนคลายเลาะสวนจิตรฯ