FOR COMMUNITY NEUROLOGISTS: WOMEN WITH EPILEPSY

CONTRACEPTION

Enzyme-inducing anti-epileptic drugs (AEDs) such as phenytoin (PHT), carbamazepine (CBZ) and phenobarbital (PB), as well as topiramate (TPM) (> 200 mg/day) and oxcarbazepine (OXC) may increase the failure rate of oral contraception. CBZ decreases levels of contraceptive steroids, increases breakthrough bleeding and does not adequately protect women from pregnancy[1]. Enzyme-inducing AEDs should be avoided (if possible) in women with epilepsy who are using oral contraceptives, transdermal patches, or levonorgestrel implants. Oral contraception may reduce levels of lamotrigine (LTG). Intrauterine devices do not appear to interact with AEDs.

PRE-CONCEPTION AND PREGNANCY

- Since women whose seizures are well-controlled are likely to remain seizure-free during pregnancy, physicians should aim for seizure freedom prior to pregnancy.
- If possible, the AED regimen during pregnancy should be simplified to monotherapy at the lowest dose[3].
- Folic acid supplements (1-5 mg/day) are recommended before and during pregnancy to reduce the risk of midline birth defects and low IQ in the offpsring of women with epilepsy.
- Women with epilepsy who smoke may be at greater risk of premature contractions and premature labour and delivery. Smoking cessation is encouraged.

Exposure to valproic acid (VPA) during pregnancy is associated with birth defects including spina bifida, autism spectrum disorders, and lower verbal IQ. Women taking VPA who are thinking of becoming pregnant should change to another AED well before pregnancy as the risk of major congenital malformations occurs very early in pregnancy[3].

- Topiramate is associated with an increased risk of facial clefts[4,5]. Neonates born to women with epilepsy taking AEDs have a higher risk of having a small for gestational age birthweight and having a one-minute Apgar score of <7[3].
- PB, primidone (PRM), PHT, CBZ, levetiracetam (LVT) and VPA likely cross the placenta at potentially clinically significant levels. Gabapentin (GBP), LTG, OXC and TPM possibly cross the placenta as well[2].
- Pregnancy is associated with a decrease in LTG, CBZ, and PHT levels[2]. AED levels should be determined during each trimester of pregnancy.

BREASTFEEDING

PRM and LVT likely penetrate into breast milk in potentially clinically significant amounts. GBP, LTG and TPM possibly penetrate into breast milk while VPA, PB, PHT and CBZ probably do not. However, there is insufficient evidence to link AEDs ingested through breast milk to clinically significant outcomes[2]. Breastfeeding is not contraindicated.

MENOPAUSE

Women who are menopausal and taking enzyme-inducing AEDs may be at greater risk of bone fractures[6] and should undergo regular screening for osteoporosis. Daily Vitamin D and calcium supplements are recommended. Ideally, enzyme-inducing AEDs should be avoided in women at risk for osteoporosis.

KEY POINTS

- Discuss plans for pregnancy with women of childbearing age
- Avoid enzyme-inducing AEDs in women with epilepsy using oral contraceptives, transdermal patches, or levonorgestrel implants
- Exposure to VPA during pregnancy is associated with birth defects including spina bifida, autism spectrum disorders, and lower verbal IQ
- Folic acid supplements (1-5 mg/day) are recommended before and during pregnancy
- Toronto Western Hospital offers a specialized epilepsy and pregnancy clinic. More information on referrals to this clinic can be found at: www.OntarioEpilepsyGuidelines.ca/pregnancy-clinic

References

(1) Davis AR, Westhoff CL & Stanczyk FZ. Carbamazepine co-administration with an oral contraceptive: effects on steroid pharmacokinetics, ovulation and bleeding. Epilepsia 2001; 52(2): 243-247.

(2) Harden CL et al. Practice Parameter update: Management issues for women with epilepsy -- Focus on pregnancy (an evidence-based review): Vitamin K, folic acid, blood levels, and breastfeeding. Neurology 2009b; 73(2): 142-149.

(3) Harden CL et al. Practice Parameter update: Management issues for women with epilepsy -- Focus on pregnancy (an evidence-based review): Teratogenesis and perinatal outcomes. Neurology 2009a; 73(2): 133-141.

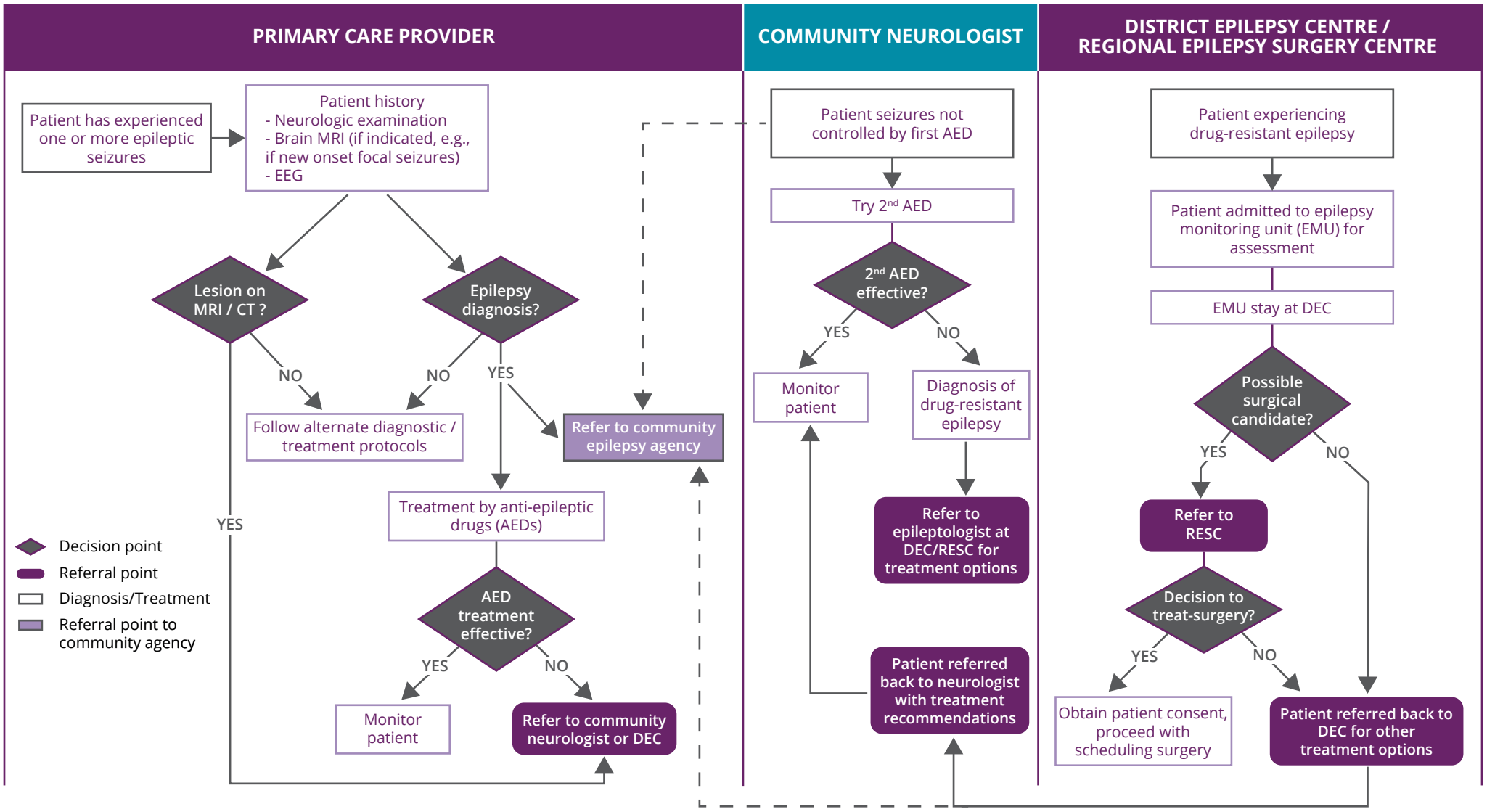
(4) Hunt S et al. Topiramate in pregnancy. Neurology 2008; 71(4):472-476

(5) Margulis AV et al. Use of topiramate in pregnancy and risk of oral clefts. American Journal of Obstetrics and Gynecology 2012; 207(5): 405.e1-405.e7

(6) Brodie MJ et al. Enzyme Induction with antiepileptic drugs: Cause for concern? Epilepsia 2013; 54(1): 11-27

Recommendations from the Epilepsy Implementation Task Force (EITF), supported by Critical Care Services Ontario

EPILEPSY PATIENT REFERRAL PATHWAY



Local Health Integration Network (LHIN)	PEDIATRIC		ADULT	
	DEC	RESC	DEC	RESC
Erie St. Clair	LHSC	LHSC	LHSC	LHSC
South West	LHSC	LHSC	LHSC	LHSC
Waterloo Wellington	HHS	SickKids	LHSC/HHS	LHSC
HNHB	HHS	SickKids	HHS	LHSC
Central West	SickKids	SickKids	UHN	UHN
Mississauga Halton	SickKids	SickKids	UHN	UHN
Toronto Central	SickKids	SickKids	UHN	UHN

Local Health Integration Network (LHIN)	PEDIATRIC		ADULT	
	DEC	RESC	DEC	RESC
Central	SickKids	SickKids	UHN	UHN
Central East	SickKids	SickKids	UHN	UHN
South East	KHSC	SickKids	KHSC	UHN
Champlain	CHEO	SickKids	TOH	UHN
North Simcoe Muskoka	SickKids	SickKids	UHN	UHN
North East	CHEO	SickKids	LHSC	LHSC
North West	LHSC	LHSC	LHSC	LHSC

Note: This referral pathway has been endorsed by the EITF and Provincial Neurosurgery Advisory Committee (PNAC). These recommendations are not intended to supersede existing referral relationships. Referring practitioners are encouraged to check with DECs for average wait times when making referrals. Where possible, it is suggested to offer patients options to enhance their timely access to care.

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