SEIZURES IN PREGNANCY

FLAME LECTURE: 38

CONOVALOFF/STELLER 8.11.19

LEARNING OBJECTIVES

- Describe how certain medical conditions (seizures) affect pregnancy
- Describe how pregnancy affects certain medical conditions (seizures)
- Identify the following medical and surgical conditions in pregnancy and discuss the potential impact of the conditions (seizures) on the gravid patient and the fetus/newborn, as well as the impact of pregnancy (if any) on each condition, and the appropriate initial evaluation: neurologic disease
- Prerequisites:
  - NONE
- See also – for closely related topics
  - FLAME 106 - ECLAMPSIA

BACKGROUND

- Seizures are characterized by abnormal yet synchronized, high-frequency neuronal firing
- Epilepsy is defined as recurrent, unprovoked seizures
- Causes of seizures in adults: tumors, infection, trauma, stroke
- Focal seizures originate in a specific locus in the brain and include:
  - Automatisms (ex. lip-smacking) and can be motor, sensory, or autonomic
- Diffuse seizures are described in a number of ways:
  - Grand mal – alternating stiffening and movement
  - Tonic – stiffening
  - Atonic – "drop" seizures
  - Myoclonic – repetitive jerks

CLINICAL CONSEQUENCES
MATERNAL

- Over 90% of women with epilepsy do not have complications during pregnancy
  - However, there are slightly increased risks of gestational hypertension, preeclampsia, preterm labor, placental abruption, postpartum hemorrhage, and cesarean delivery (OR 1-1.5)
  - There is also an increased risk of peripartum depression and anxiety
    - All practitioners should be advised to screen pregnant patients with a history of seizures periodically during the antepartum and postpartum periods as well as provide appropriate referrals when necessary

CLINICAL CONSEQUENCES
MATERNAL

- 10x higher risk of maternal mortality for those with seizures as compared to the general population
  - However, this is an absolute risk increase of < 0.1%
- Inconclusive evidence to suggest pregnancy augments the number OR severity of seizures
  - Though altered pharmacokinetics or compliance with medications during pregnancy have been proposed concerns
- Seizures are more likely to occur in peripartum period
  - Highest risk time period is immediately surrounding delivery

CLINICAL CONSEQUENCES
FETAL

- There are slightly increased risks of prematurity (given an elevated risk of preterm delivery) as well as fetal growth restriction
- A slightly increased risk of intrauterine fetal demise / stillbirth
  - Risk of stillbirth is 0.8% in mothers with seizures vs. 0.6% in the general population
- The largest concern is the acute effects of maternal seizures on the fetus given there may be decreased placental flow and oxygen delivery during a seizure
  - This may acutely lead to fetal bradycardia or placental abruption

MEDICATION CONCERNS

- Anti-epileptic medications, regardless of disorder being treated, increase the risk for preterm birth and small for gestational age infants, HOWEVER, as on the previous slides, so does withholding treatment
- 2-3% absolute risk increased of major congenital malformations
  - Most common: Neural tube defects, heart abnormalities, urinary tract deformities, skeletal abnormalities, oral clefts
  - **Valproic acid** carries highest risk of malformations (commonly neural tube defects)
  - Phenytoin, phenobarbital also carry high risk of the above anomalies
  - Carbamazepine, topiramate, zonisamide carry a moderate risk
  - Lamotrigine, levetiracetam, oxcarbazepine have lowest risk
    - >200-325 mg/day lamotrigine may increase risk

MEDICATIONS (CONT'D)

- *In utero* exposure to anti-epileptic medications are also associated with impaired cognitive and behavioral development, autism spectrum disorders
  - Most significant with valproic acid
- Supplemental folic acid recommended in all pregnant women (400-600 mcg/day), but especially in pregnant women taking anti-epileptic medication (up to 4 g/day)
  - Increased mean IQ of six-year-old children for mothers who took periconceptional folic acid
  - Folic acid doses inversely correlated with autism severity
- When/if attempting to decrease dose or number of anti-epileptic medications during pregnancy, this must always be balanced with the risk of inadequate treatment and seizures on mother and fetus

CONTRACEPTION CONSIDERATIONS

- Most anti-epileptic medications are hepatic enzyme inducers which can affect hormonal agents and increase risk of contraception failure → unplanned pregnancy
  - *Strong*: carbamazepine, oxcarbazepine, perampanel, phenobarbital, phenytoin, primidone
  - *Weak*: clobazam, eslicarbazepine, felbamate, lamotrigine, rufinamide, topiramate
- LARCs such as the copper or levonorgestrel IUDand DMPA are preferred over CHCs such as pill/patch/ring

MANAGEMENT OF ACUTE SEIZURE

- Move patient to left lateral decubitus and raise bed rails
- Mobilize team (OB, Anesthesia, nursing, alert NICU if still pregnant, Neurology)
- Check ABCs and vitals, start supplemental O_2, obtain IV access
- If fetus of viable gestational age, initiate fetal heart rate monitoring and tocometry
- Determine etiology of the seizure
  - Glucose, electrolytes, tox screen, HELLP labs
  - ALWAYS consider eclampsia, even in a patient with known epilepsy (see next slide)

ECLAMPSIA SIDETRACK

- See FLAME 106 for a detailed presentation on eclampsia
- Eclamptic seizures ALSO are at peak incidence in the days surrounding delivery
- They occur in 0-0.6% of women with preE w/o severe features, and 2-3% of women with preE with severe features
- Seizures typically last < 2 mins, but may last up to 4 mins
- If ANY possibility the seizure is 2/2 eclampsia, just administer magnesium sulfate 6g IV (or 10g IM) bolus!
- Evaluate for other evidence of pre-eclampsia (elevated BPs, abnormal Hgb, platelets, creatinine, LFTs, abnormal DTRs on physical exam)
- Delivery is the only definitive long-term management strategy

Now BACK TO ACUTE MANAGEMENT →

MANAGEMENT OF ACUTE SEIZURE

- If glucose <60 mg/dL, give 100 mg thiamine IV and 50 ml D50W IV
- If not eclampsia, choose one of the following 1st line options to try and break the seizure:
  - IM midazolam (10 mg for >40 kg, 5mg for 13-40 kg)
  - IV diazepam (0.15-0.2 mg/kg/dose, max: 10 mg/dose)
  - IV lorazepam (0.1 mg/kg/dose, max: 4 mg/dose)
- If none of these 3 options are available, consider:
  - Rectal diazepam (0.2-0.5 mg/kg, max: 20 mg/dose)
  - Intranasal/buccal midazolam
  - IV Phenobarbital (15 mg/kg/dose) *if you must*
- If known history of epilepsy, Neurology may consider increasing dose of current medication, or adding another anti-epileptic

DIFFERENTIAL DIAGNOSIS

- If the patient doesn't have a known seizure disorder and its not eclampsia, lastly consider:
  - Meningeal irritation (brain bleed, infection, trauma, tumor)
  - Metabolic disturbance (hyponatremia, hypocalcemia, hypoglycemia, uremia)
  - Toxic ingestion, overdose, or alcohol intoxication
  - Neurodegenerative disorder or autoimmune disease

IMPORTANT LINKS / REFERENCES

- UpToDate
- First Aid Step 2 CK
- Bromfield EB, Dworetzky BA, Wyszynski DF, et al. Valproate teratogenicity and epilepsy syndrome. Epilepsia 2008; 49:2122.
- Meador KJ, Baker GA, Browning N, et al. Fetal antiepileptic drug exposure and cognitive outcomes at age 6 years (NEAD study): a prospective observational study. Lancet Neurol 2013; 12:244.
- Sabers A. Influences on seizure activity in pregnant women with epilepsy. Epilepsy Behav 2009; 15:230.
- Tomson T, Battino D. Teratogenic effects of antiepileptic drugs. Lancet Neurol 2012; 11:803.
- https://www.aesnet.org/clinical_resources/guidelines