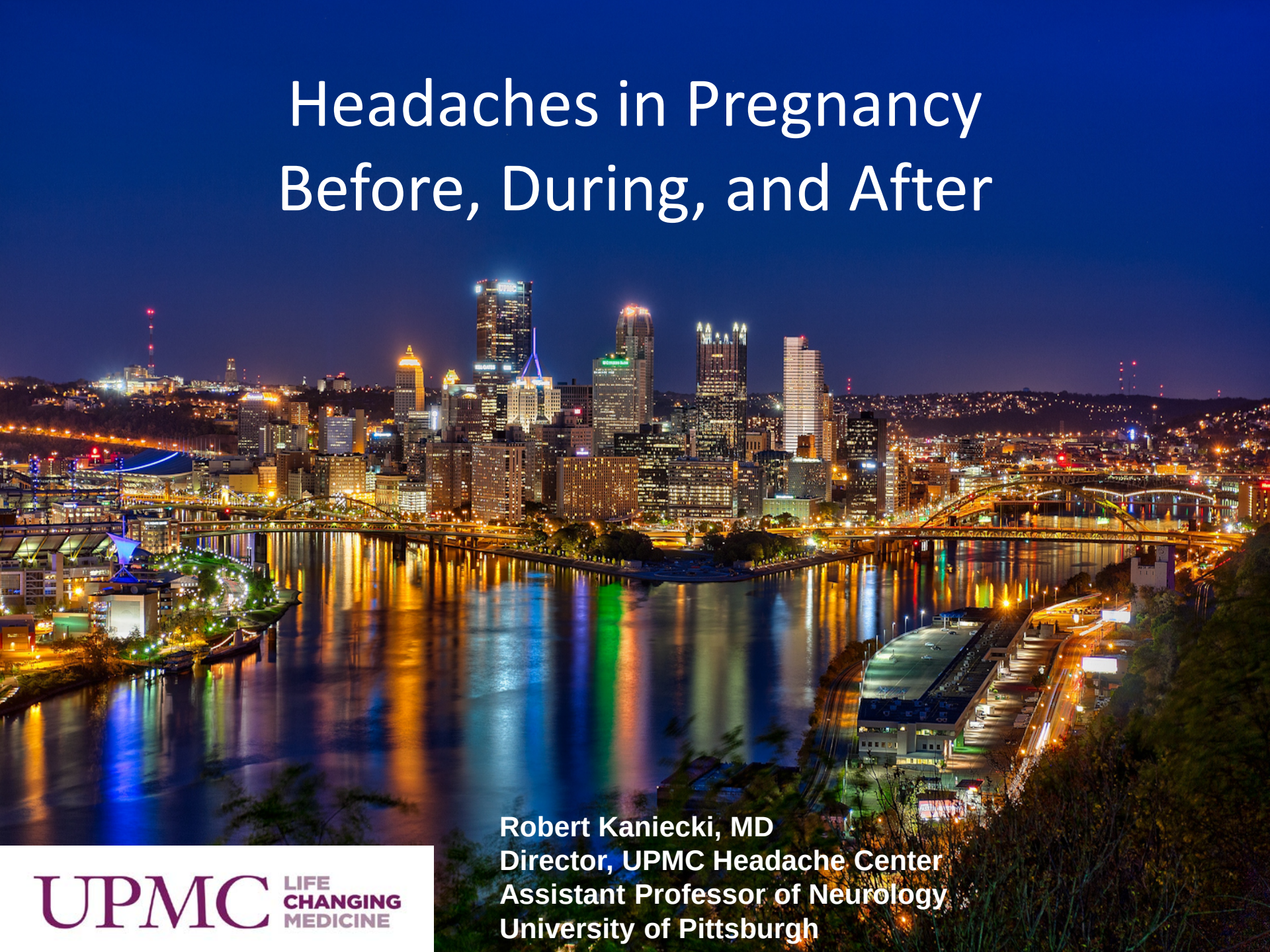
Headaches in Pregnancy Before, During, and After



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UPMC LIFE CHANGING MEDICINE

Headaches and Pregnancy

- Pre-pregnancy counseling
- Headaches in pregnancy
- Post-partum headaches

Headaches and Pregnancy

- Exposure during pregnancy to which of the following agents is associated with fetal congenital heart defects:
  - A. Topiramate
  - B. Sumatriptan
  - C. Magnesium sulfate
  - D. Butalbital

Headaches and Pregnancy

- Which of the following clinical features provides the greatest risk for a secondary headache presentation during pregnancy:
  - A. Hypertension
  - B. Absence of previous headache history
  - C. Seizures
  - D. Fever
  - E. Abnormal neurological examination

Headaches and Pregnancy

- A 23yo woman in her early third trimester presents with progressive daily headaches over 6 weeks. Her exam shows papilledema but is otherwise normal. The next most appropriate step in management should be:
  - A. Head CT
  - B. Lumbar puncture
  - C. Brain MRI
  - D. Acetazolamide

Headaches and Pregnancy

- A 25yo woman is breastfeeding but requires migraine prophylaxis. Which of the following agents is most appropriate:
  - A. Atenolol
  - B. Topiramate
  - C. Metoprolol
  - D. Sodium valproate

Pre-pregnancy Counseling

Pre-pregnancy Counseling

- Maximize non-pharmacological management
- Adjust pharmacological measures
- Address
  - Potential impact of pregnancy on migraine
  - Potential impact of migraine on pregnancy

Lifestyle Recommendations
Throughout Pregnancy Course

- Schedule regulation
  - Sleep regular hours, avoiding naps
    - Minimize screen exposure
  - Meals/snacks: 4-6 small portions daily
  - Exercise daily
  - Hydration – minimum 2 liters (60 ounces) daily
  - Regular school/work attendance
- Minimize caffeine and analgesic intake
- “Trigger” avoidance

Non-pharmacologic Options
Throughout Pregnancy Course

- Magnesium supplementation (500mg) often advised
  - Prolonged maternal IV magnesium sulfate associated with fetal bone demineralization
  - Magnesium glycinate of gluconate considered best options
- Neurostimulators not adequately studied
  - Supraorbital simulaor
  - Noninvasive vagus nerve stimulator
  - Single pulse transcranial magnetic stimulator

Non-pharmacologic Options

Throughout Pregnancy Course

- Relaxation training, thermal and electromyographic biofeedback, and cognitive-behavioral approaches (Grade A)
- Behavioral therapy may enhance effectiveness of preventive drug therapy (Grade B)
- Data insufficient for acupuncture, hypnosis, TENS, chiropractic/osteopathic manipulation

AAN Practice Parameters, Copyright 2000; 538-547

Optimize Pharmacological Safety Profile

- Acute medications
- Preventive medications
- Interventional procedures

Acute Migraine Medications

- Medication (Evidence)
  - Acetaminophen (A*)
  - Ibuprofen, Naproxen (A)
  - Aspirin (A)
  - Triptans (A)
  - Butorphanol (A, C*)
  - Butalbital (C)
  - Prochlorperazine (B*)
  - Metoclopramide (B*)
- FDA pregnancy rating
  - B
  - C (D after 30 weeks)
  - D (high dose)
  - C
  - C
  - C
  - C
  - B

Wells et al. Curr Neurol Neurosci Rep 2016;16:40

Migraine Preventive Medications

- Medication (Evidence)
  - Sodium valproate (A)
  - Topiramate (A)
  - Amitriptyline (B)
  - Venlafaxine (B)
  - Propranolol (A)
  - Metoprolol (A)
  - Timolol (A)
  - Atenolol (B)
- FDA pregnancy rating
  - D
  - D
  - C
  - C
  - C
  - C
  - C
  - D

Wells et al. Curr Neurol Neurosci Rep 2016;16:40

Interventional Therapies

- Pericranial nerve blocks
  - Lidocaine (B)
  - Bupivacaine (C)
- Botulinum toxin (C)
  - High molecular weight – low likelihood of placenta crossing
  - No increased rates of fetal loss or birth defects (n=232)
- Monoclonal antibodies versus CGRP or CGRP-receptor
  - Also large molecules with low risk or placental transfer
  - Unknown risks

Morgan et at J Neurol Neurosurg Psychiatry 2006

Headaches in Pregnancy

Headache Classification

Primary Headaches

- Migraine
- Tension-type
- Cluster
- Other primary headaches

Secondary Headaches

- Trauma
- Vascular disorders
- Non-vascular intracranial disorder
- Substances/withdrawal
- Infection
- Disorder of homeostasis
- Disorder of extracranial structures
- Psychiatric disorder
- Cranial neuralgia

ICDH-3 beta Cephalalgia 2013;33:609-828

Profiling Secondary Headache
Red Flags

- First/worst headache
- Abrupt onset headache
- Progression or fundamental change in pattern
- New headache in those <5yo, >50yo
- New headache in high-risk clinical settings
- Headache with syncope or seizure
- Headache triggered by exertion/valsalva/sex
- Neurologic symptoms >1hour in duration
- Abnormal general or neurological examination

Headaches in Pregnancy
Screening for Secondary Headaches

- Headaches in pregnancy
  - 5% affected by *new* headache or headache type

Spierings et al. Neurologist 2016; 21:1-7.

Acute Headache in Pregnancy

- Primary headache 65%
  - Majority (59.3% of total population) migraine
- Secondary headache 35%
  - Hypertensive disorders of pregnancy

Robbins et al. Neurology 2015;85:1024-1030

Acute Headache in Pregnancy

- Factors associated with secondary headache
  - Hypertension (17-fold increase)
  - Absence of headache history
  - Seizures
  - Fever
  - Abnormal neurological examination
  - Longer primary headache attack duration

Robbins et al. Neurology 2015;85:1024-1030

Pregnancy-specific Considerations

Primary Headaches

- Migraine
- Tension-type

Secondary Headaches

- Preeclampsia/eclampsia
- RCVS
- Intracranial hemorrhage
- IIH
- Intracranial tumor
- Venous/sinus thrombosis
- Stroke
- Pituitary apoplexy
- Chiari malformation

Workup of Potential Secondary Headache

- Neuroimaging
  - ED/Acute – Head CT
  - Outpatient/subacute – MRI
  - Low threshold for MRA and MRV
- Special settings
  - LP

Acute Headache in Pregnancy
Imaging

- 151 pregnant women with acute headache
  - 50% underwent neuroimaging
  - Symptomatic pathology found in 27.6%
    - Increased risks with
      - First trimester headache
      - Strong pain intensity
      - Reduced level of consciousness
      - Seizure

Raffaelli et al. Journal of Neurology 2018;265:1836-1843

Diagnostic Procedures

Test	Risk to Mother	Risk to Fetus	Contraindication
EEG	None	None	None
Ultrasound	None	None	None
Duplex-Doppler	—	—	—
Orbital (A/B scan)	—	—	—
Echocardiogram	—	—	—
Lumbar puncture	None	None	Incipient herniation
Head CT	None	Minimal*	None
Head CT with contrast	None	Minimal*	Dye allergy
Head CTA and CTV	None	Minimal*	Dye allergy
Angiography	None	Minimal*	Dye allergy
Head MRI	None	None known	Metal, devices
Head MRV	None	None known	Metal, devices
VF	None	None	None

*With abdominal shielding.

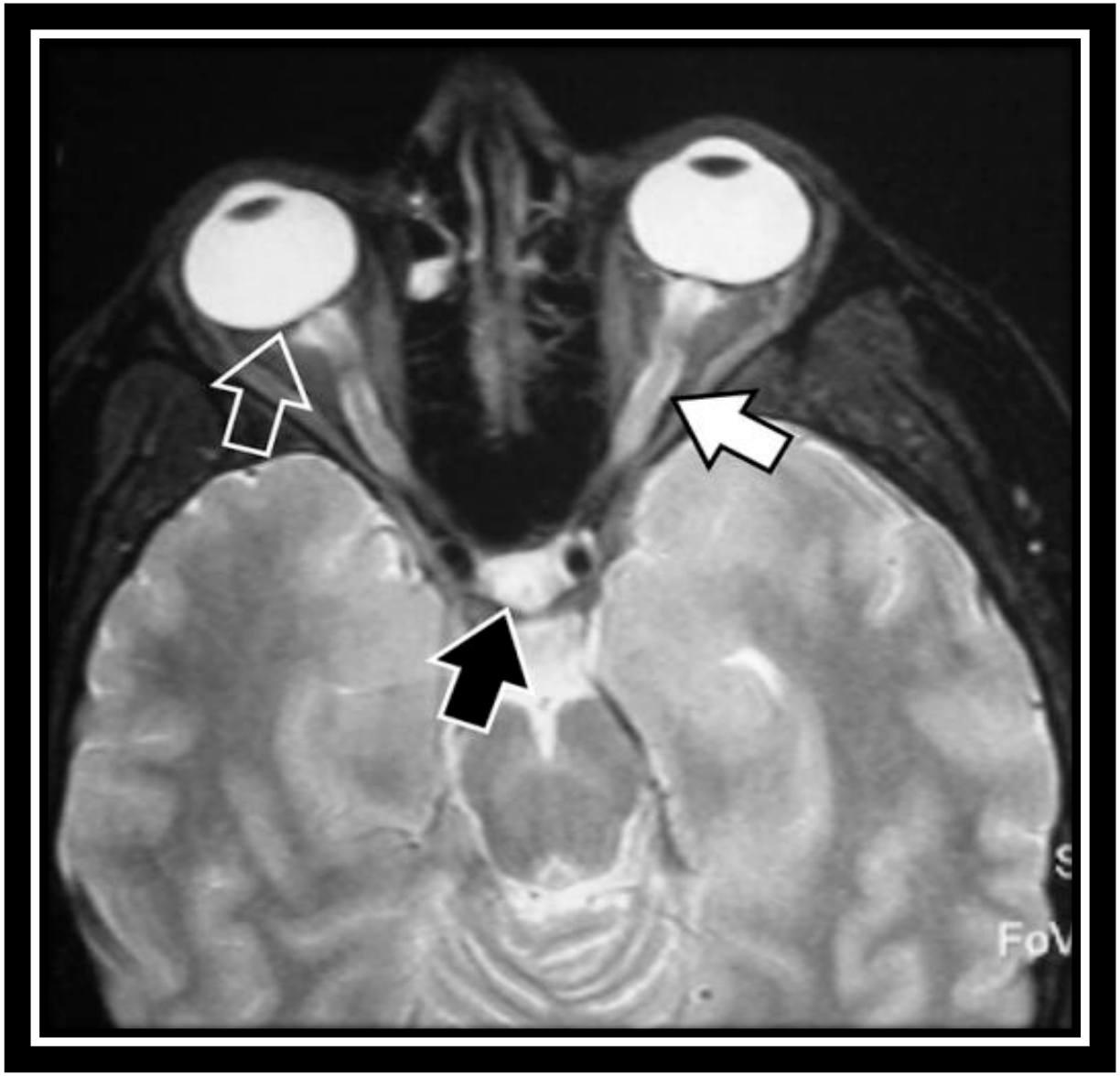
CT indicates computed tomography; CTA, computed tomography arteriogram; CTV, computed tomography venogram; EEG, electroencephalography; MRI, magnetic resonance imaging; MRV, magnetic resonance venography; VF, visual field.

Adapted in part from Digre et al.[3]

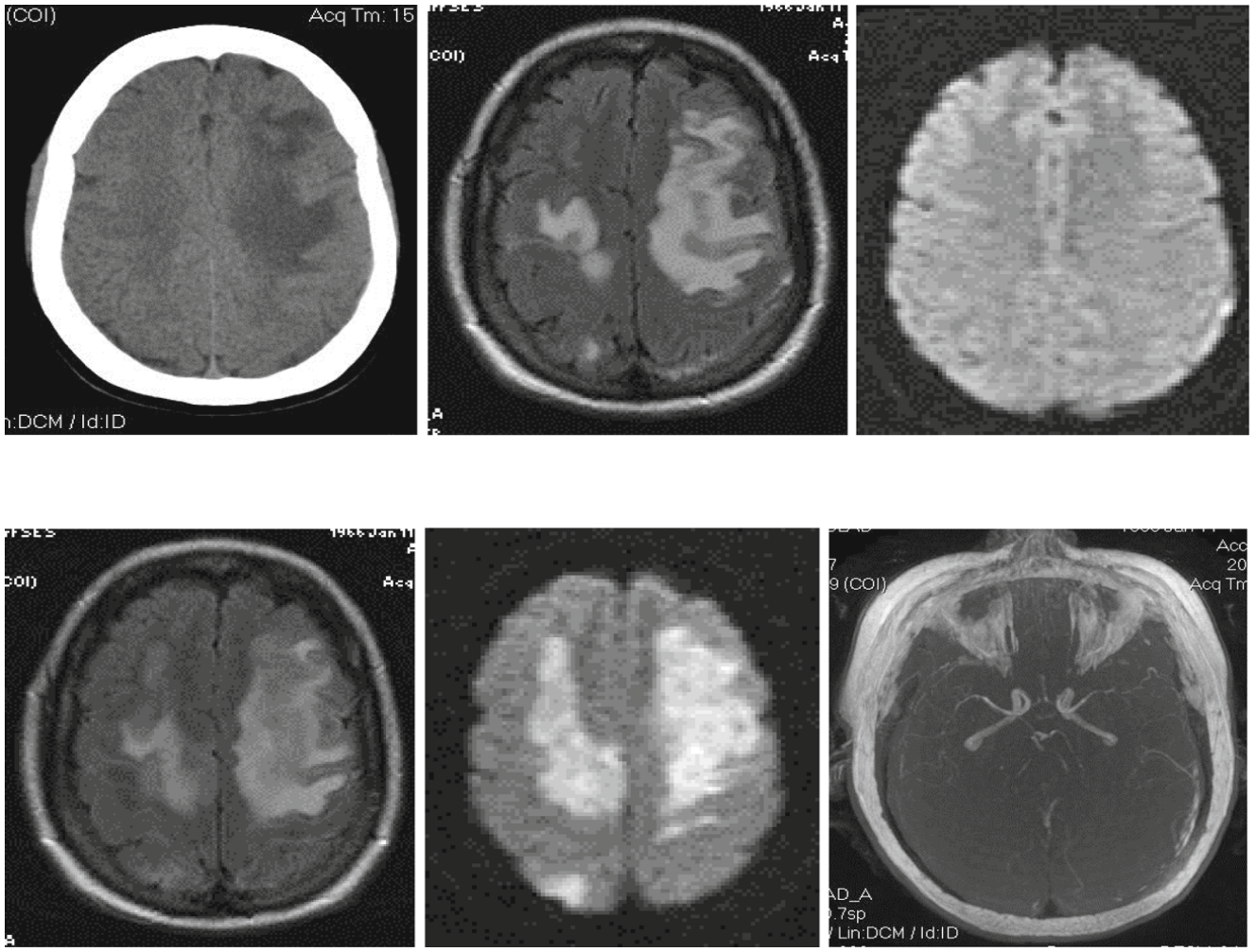
CT contrast FDA class B, gadolinium class C

Digre. Clin Obstet Gynecol 2013;56:317-329

Idiopathic Intracranial Hypertension

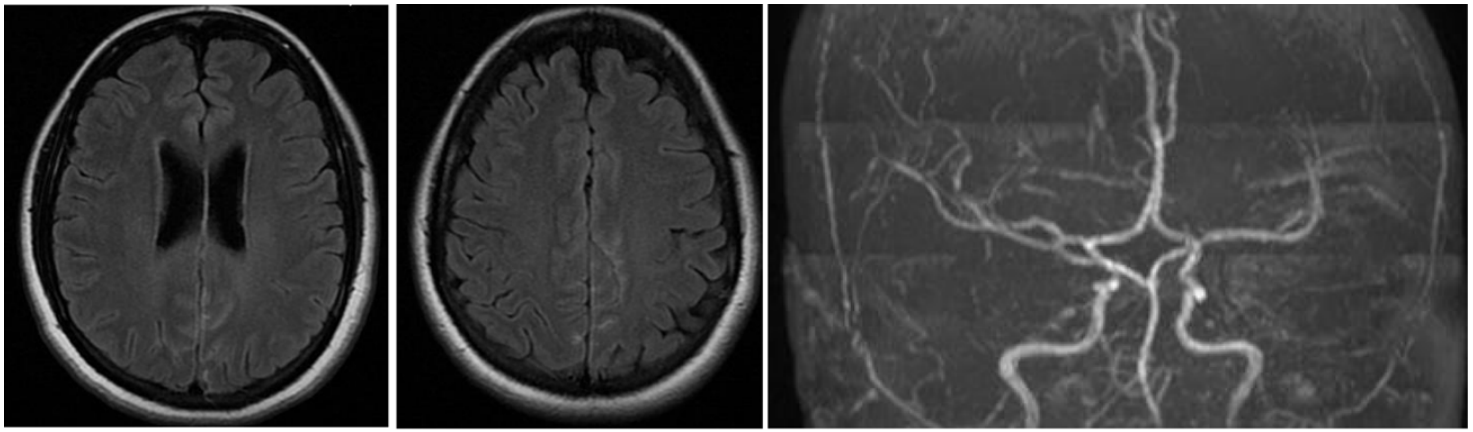


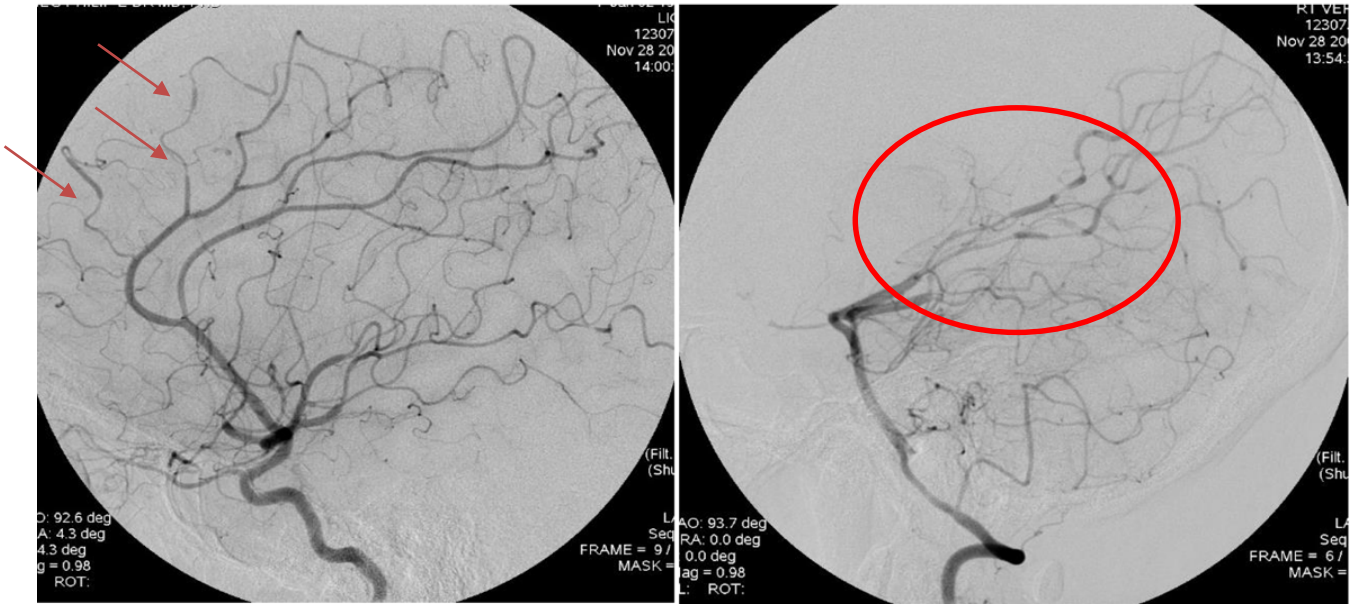
Preeclampsia



Skliut. Curr Pain Headache Rep 2016;20:56

RCVS





Skliut. Curr Pain Headache Rep 2016;20:56

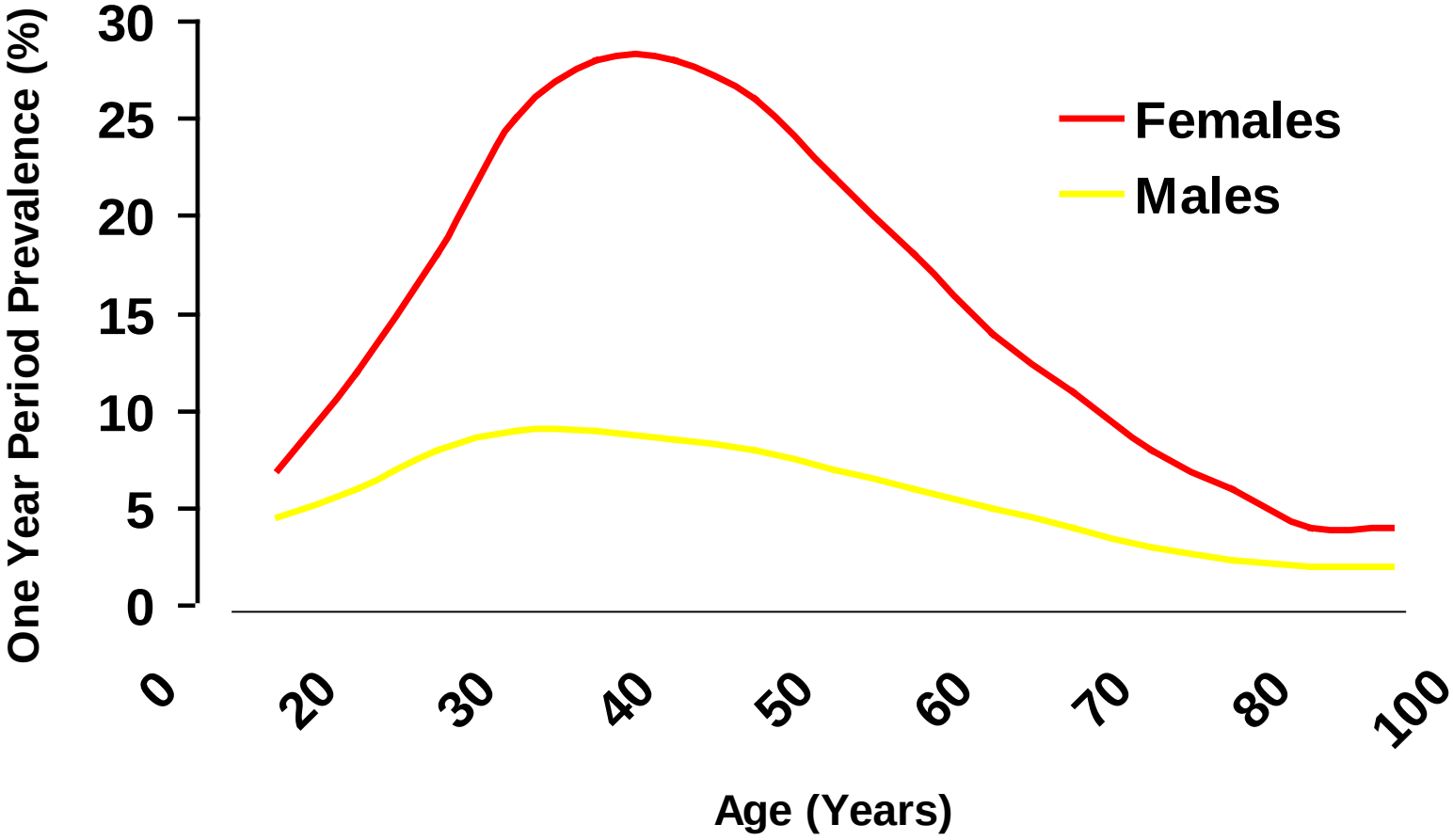
Pregnancy and Migraine

- Migraine affects approximately 25% of women of reproductive age
- Although many improve during pregnancy, approximately 25% have moderate to severe levels of migraine-related disability in the first trimester

Frederick et al. Headache 2014;54:675-685

Migraine Headache

Population prevalence



Recognizing Migraine
Diagnostic criteria

- 1.1 Migraine without aura
  - At least 5 attacks (4-72 hours)
  - Pain features (at least 2)
    - Unilateral
    - Pulsating
    - Moderate to severe intensity
    - Aggravated by activity
  - Associated features (at least 1)
    - Nausea and/or vomiting
    - Photo and phonophobia
  - No organic disease

ICHD-3 beta Cephalalgia 2013;33:609-828

Recognizing Aura
Diagnostic criteria

- 1.2 Migraine with Aura
  - At least 2 attacks
  - Aura consisting of at least one of the following
    - **Fully reversible** visual symptoms
    - **Fully reversible** sensory symptoms
    - **Fully reversible** dysphasic symptoms
  - At least 2 of the following
    - Hemifield or hemisensory symptoms
    - Development over 5 minutes
    - Each symptom last **>5 and <60 minutes**
  - Headache fulfilling criteria for Migraine without aura begins during or follows aura within 60 minutes

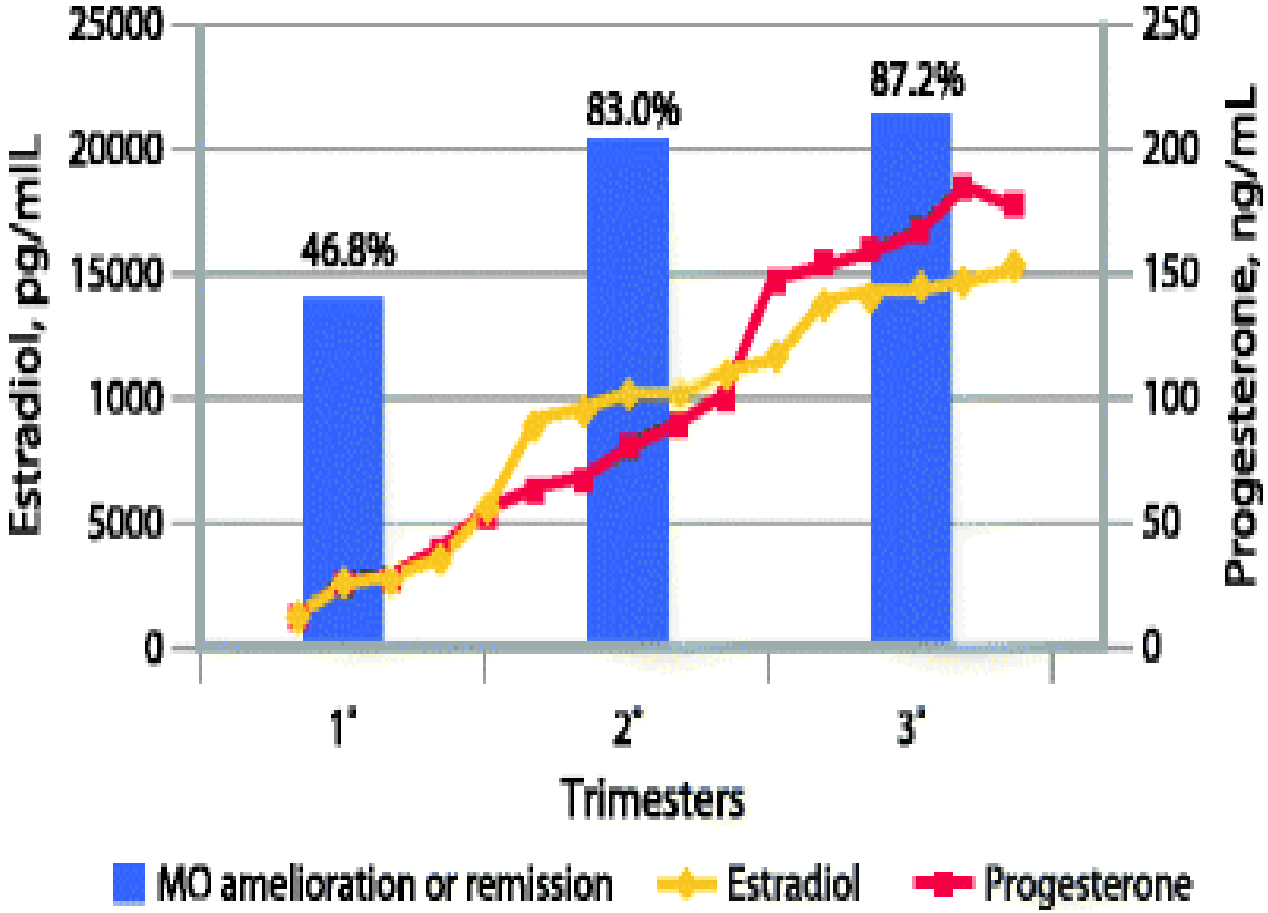
ICHD-3 beta Cephalalgia 2013;33:609-828

Effects of Pregnancy on Migraine

- Migraine without aura typically improves
- Migraine with aura typically does not

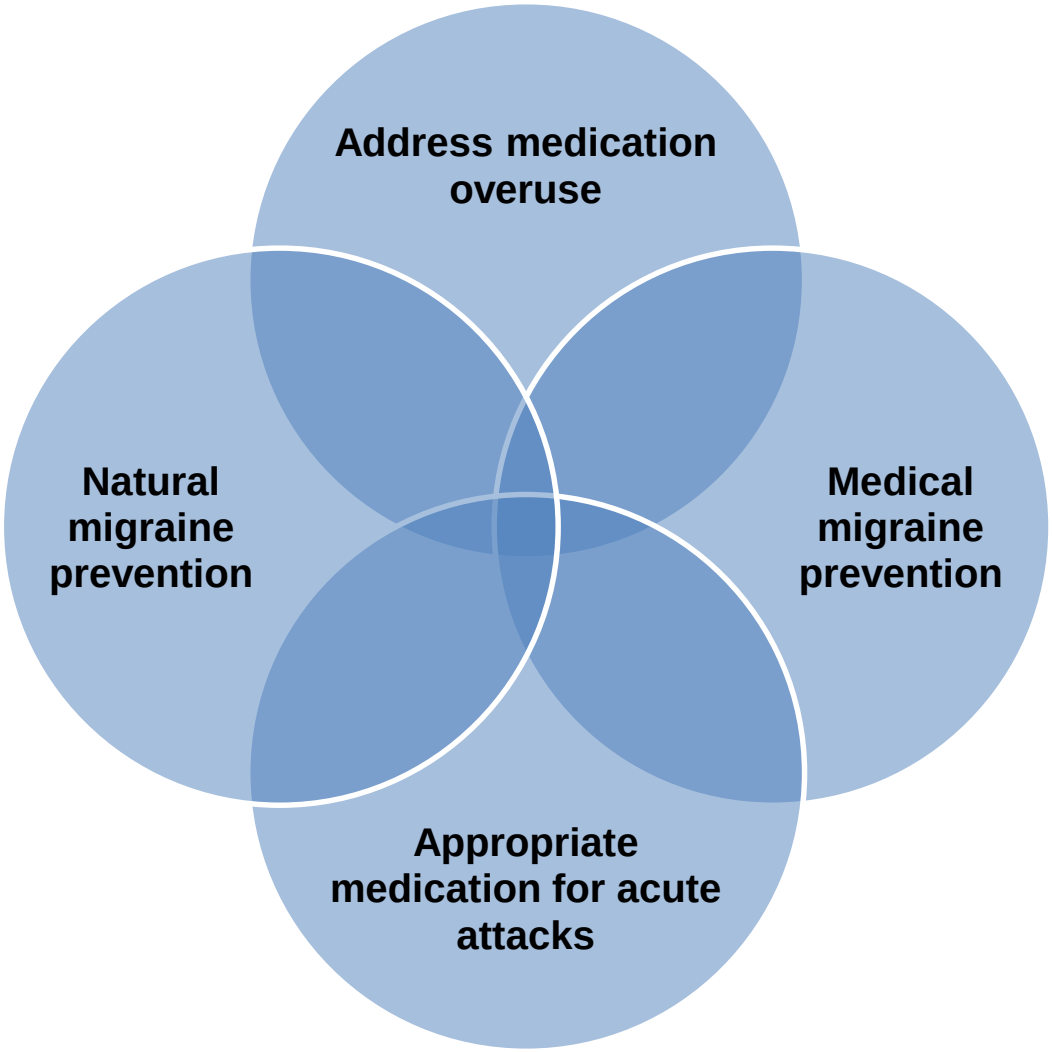
- Migraine may develop during pregnancy
  - More common in those with aura

Course of Migraine without Aura



Nappi et al. Curr Pain Headache Rep 2011;15:289

Management of Migraine



Acute Migraine Management in Pregnancy
Clinical practice

- First-line agents
  - Acetaminophen 1000mg (caffeine)
    - Metoclopramide 10mg
    - Ondansetron 4mg
- Second-line agents
  - Sumatriptan 100mg tablets or 4,6mg injections
    - Triptan with the greatest amount of data/experience
    - Most hydrophilic triptan
  - Prochlorperazine, ibuprofen, other triptans

Robbins M. Continuum 2018;24:1092-1107
Calhoun A. Curr Pain Headache Rep 2017;21:46

Acute Migraine Management in Pregnancy
Clinical practice

- Emergency Department management
  - Acetaminophen 1000mg IV
  - Metoclopramide 10mg IV
  - Diphenhydramine 25mg IV
  - IV fluids

Robbins M. Continuum 2018;24:1092-1107
Childress K et al. Amer J Perinat 2018

Acute Migraine Management in Pregnancy
Clinical practice

- Avoid if at all possible:
  - Opioids – nausea, inflammation, MOH
  - Butalbital – congenital heart defects, MOH

Robbins M. Continuum 2018;24:1092-1107
Calhoun A. Curr Pain Headache Rep 2017;21:46

Triptans in Pregnancy
Clinical experience

- Sumatriptan FDA approval 1992
- Triptans are used by 15-25% of pregnant women with migraine

Amundsen et al. Eur J Clin Pharmacol 2016;72:1525-1535

Triptans in Pregnancy
Clinical Data

- Triptan registry information
  - No significant increase in major congenital malformations

Ephross et al. Headache 2014;54:1158-1172

Triptans in Pregnancy
Clinical Data

- Meta-analysis of 6 studies (4208 exposures)
  - No increased risk of malformations or prematurity
  - Increased rate of spontaneous abortions
  - Increased rate of major congenital malformations in the non-triptan migraine subgroup

Marchenko et al. Headache 2015;55:490-501

Triptans in Pregnancy
Clinical Data

- Prospective observational cohort study
  - German Embryotox system
  - 432 pregnant women exposed to triptans
    - 70% first trimester
  - No differences in
    - Major birth defects
    - Spontaneous abortions
    - Preterm delivery
    - Preeclampsia

Spielmann et al. Cephalalgia 2018

Triptans in Pregnancy
Clinical Data

- Prospective observational cohort study
  - Norwegian Mother and Child Cohort Study
  - 3784 children
    - 1922 (51%) mothers migraine prior to pregnancy
    - 1509 (40%) migraine with pregnancy, no triptan
    - 353 (9.3%) migraine with pregnancy, with triptan

Harris et al. Paediatr Perinat Epidemiol. 2018

Triptans in Pregnancy
Clinical Data

- Prospective observational cohort study
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  - 3784 children
    - 1922 (51%) mothers migraine prior to pregnancy
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    - 353 (9.3%) migraine with pregnancy, with triptan
  - No neurodevelopmental abnormalities at 5 years in those exposed to triptans

Harris et al. Paediatr Perinat Epidemiol. 2018

Triptans in Pregnancy
Clinical Data

- Prospective observational cohort study
  - Norwegian Mother and Child Cohort Study
  - 3784 children
    - 1922 (51%) mothers migraine prior to pregnancy
    - 1509 (40%) migraine with pregnancy, no triptan
    - 353 (9.3%) migraine with pregnancy, with triptan
  - No neurodevelopmental abnormalities at 5 years
    - Triptan-exposed children did have slightly more sociable temperaments

Harris et al. Paediatr Perinat Epidemiol. 2018

Migraine Prevention in Pregnancy
Clinical practice

- First-line agents
  - Beta blockers
  - Aspirin 81mg

  - Recent data suggest both may be safely used during pregnancy

Bergman J et al. Drug Saf 2017
Rolnik D et al. NEJM 2017;377:613-622

Migraine Prevention in Pregnancy
Clinical practice

- Second-line agents
  - Pericranial peripheral nerve blocks
    - Lidocaine (B)
  - Prednisone (C) as a “cycle breaker”
  - Low-dose Amitriptyline (C)
  - Fluoxetine (C) or Venlafaxine (C) if comorbid depression or anxiety are problematic

Bergman J et al. Drug Saf 2017
Rolnik D et al. NEJM 2017;377:613-622

Effects of Migraine on Pregnancy

- Increased risks for:
  - Gestational hypertension (OR 2.85)
  - Preeclampsia and eclampsia (OR 4.0)
  - Ischemic stroke (OR 7.9)
  - Myocardial infarction (OR 4.9)
  - Thromboembolic events (DVT 2.4, PE 3.1)

Wabnitz et al. Cephalalgia 2015;35:132-139

Post-partum Headaches

Post-partum Headaches

- Post-partum headaches
  - 40% of post-partum women with headaches
    - 10% of these incapacitating
    - Median onset day 2
    - 75% primary, 25% secondary headaches
  - Recent studies suggest rates of secondary headache may be as high as 50-75%
    - Post-dural puncture, preeclampsia

Spierings et al. Neurologist 2016; 21:1-7.
Goldsczmidt E et al. Can J Anesth 2005;52:971-977
Vgontzas A et al. Headache

Post-partum Considerations

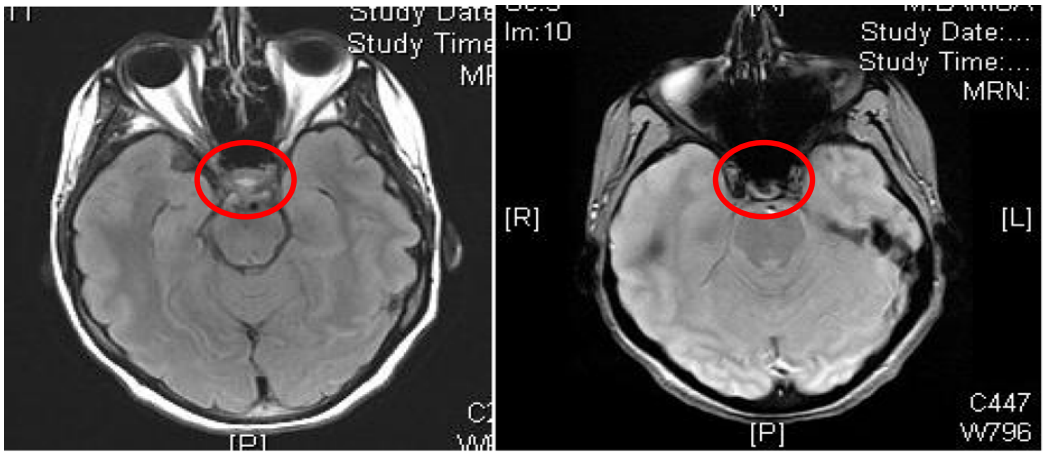
Primary Headaches

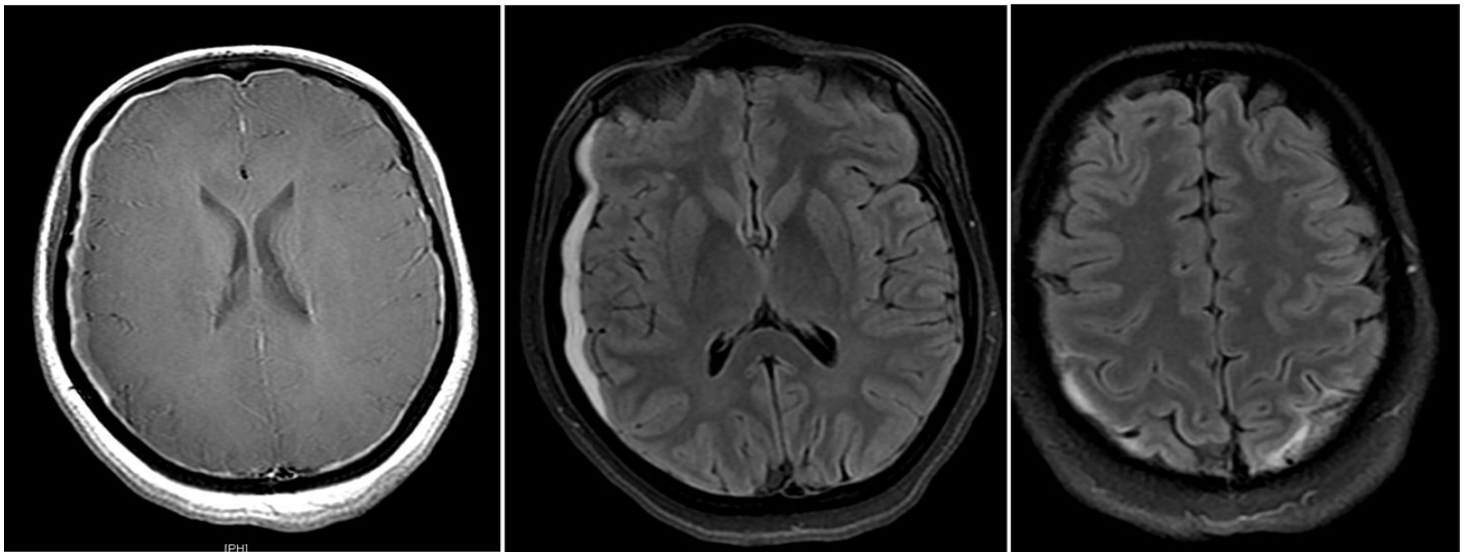
- Migraine
- Tension-type

Secondary Headaches

- Preeclampsia/eclampsia
- RCVS
- Intracranial hemorrhage
- IIH
- Intracranial tumor
- Venous/sinus thrombosis
- Stroke
- Pituitary apoplexy
- Meningitis
- Low pressure headache
- Cervical artery dissection

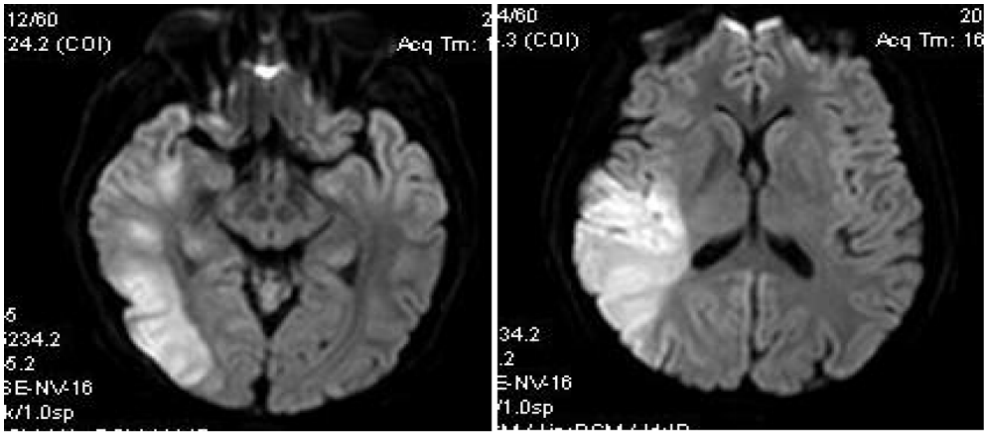
Post-partum Pituitary Hemorrhage, Post-LP Headache

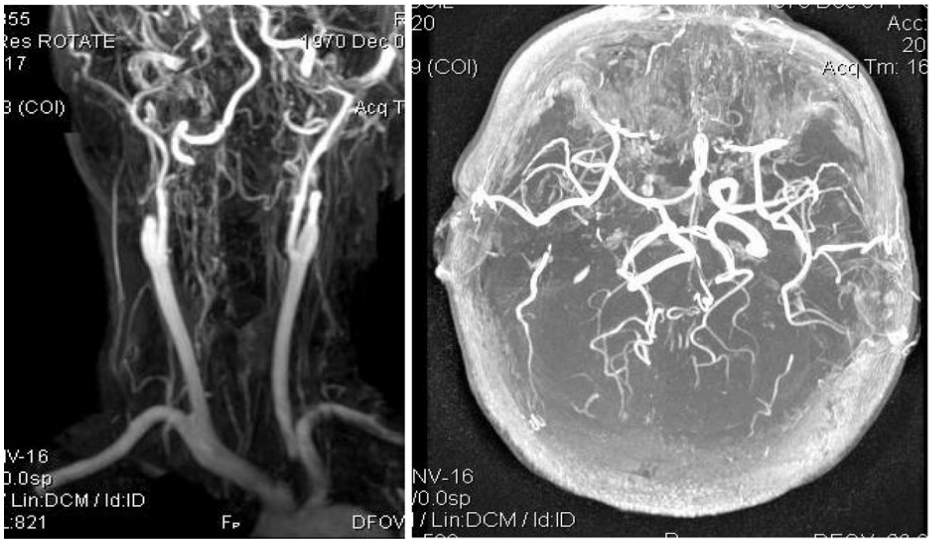




Skliut. Curr Pain Headache Rep 2016;20:56

Stroke/Carotid Dissection





Skliut. Curr Pain Headache Rep 2016;20:56

Migraine Management
Acute Medications

Medication (Evidence)	Hale lactation rating
Acetaminophen (A*)	L1
Ibuprofen, Naproxen (A)	L1, L3
Aspirin (A)	L3
Triptans (A)	L3 (Suma approved AAP)
Butorphanol (A, C*)	L2
Butalbital (C)	L3
Prochlorperazine (B*)	L3
Metoclopramide (B*)	L2

Wells et al. Curr Neurol Neurosci Rep 2016;16:40

Migraine Management
Preventive Medications

- Medication (Evidence)
  - Sodium valproate (A)
  - Topiramate (A)
  - Amitriptyline (B)
  - Venlafaxine (B)
  - Propranolol (A)
  - Metoprolol (A)
  - Timolol (A)
  - Atenolol (B)
- Hale lactation rating
  - L4
  - L3
  - L2
  - L2
  - L2
  - L2
  - L2
  - L3

Wells et al. Curr Neurol Neurosci Rep 2016;16:40

Questions