Headaches in Pregnancy
Before, During, and After

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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
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
  – B

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

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 al. 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

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

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

*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

Idiopathic Intracranial Hypertension
Preeclampsia
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

![Migraine Headache Population Prevalence Graph](image-url)
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
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

Management of Migraine

- Address medication overuse
- Natural migraine prevention
- Medical migraine prevention
- Appropriate medication for acute attacks
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
  – Prochlorperazline, ibuprofen, other triptans

Robbins M. Continuum 2018;24:1092-1107
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
Triptans in Pregnancy

*Clinical experience*

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

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

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

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  - No neurodevelopmental abnormalities at 5 years in those exposed to triptans

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Triptans in Pregnancy

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• 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

Vgontzas A et al. Headache
# Post-partum Considerations

<table>
<thead>
<tr>
<th>Primary Headaches</th>
<th>Secondary Headaches</th>
</tr>
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<tbody>
<tr>
<td>Migraine</td>
<td>Preeclampsia/eclampsia</td>
</tr>
<tr>
<td>Tension-type</td>
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<tr>
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<tr>
<td></td>
<td>Venous/sinus thrombosis</td>
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<tr>
<td></td>
<td>Stroke</td>
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<tr>
<td></td>
<td>Pituitary apoplexy</td>
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<tr>
<td></td>
<td>Meningitis</td>
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<tr>
<td></td>
<td>Low pressure headache</td>
</tr>
<tr>
<td></td>
<td>Cervical artery dissection</td>
</tr>
</tbody>
</table>
Post-partum Pituitary Hemorrhage,
Post-LP Headache
Stroke/Carotid Dissection
Migraine Management

Acute Medications

• Medication (Evidence)
  – Acetaminophen (A*)
  – Ibuprofen, Naproxen (A)
  – Aspirin (A)
  – Triptans (A)
  – Butorphanol (A, C*)
  – Butalbital (C)
  – Prochlorperazine (B*)
  – Metoclopramide (B*)

• Hale lactation rating
  – L1
  – L1, L3
  – L3
  – L3 (Suma approved AAP)
  – L2
  – L3
  – L3
  – L2

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
