HEADACHE MANAGEMENT IN EXPECTANT MOTHERS AND POST DELIVERY: EVIDENCE- BASED GUIDELINES AND BEST PRACTICES

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OBJECTIVES:

- Analyze and differentiate between primary and secondary headache
- Assess the implication of physiological changes
- Integrate interdisciplinary collaboration with comprehensive assessment and individualized patient centered plan that considers their unique maternal, emotional, and social circumstances.

CHALLENGES IN PREGNANCY

Guidelines risks vs benefits??

- Drugs not tested in pregnant individuals
- No clinical trials
- Disability
- Outcomes on maternal and fetal health
- Individualized approach
- Frequency and dosing of medication
- Combinations of medications
- Indication for use

Safety

- Loss of pregnancy
- Fetal malformation (early pregnancy)
- Developmental outcomes (late brain development stages)
- Fetal growth retardation
- Preterm birth
- Perinatal complications

PRIMARY VERSUS SECONDARY HEADACHE

Primary headache (ICHD 3)

- Is not the symptom of the underlying disease, but the condition itself
- They are caused by independent patho-mechanisms and not by other disorders

- Tension headache
- Migraine headache
- Trigeminal Autonomic Cephalgias
  - Cluster Headache
  - Paroxysmal hemicrania/Hemicrania Continua
  - Shortlasting unilateral neuralgiform headache attacks : SUNCT/SUNA
- Other Primary Headache disorders
  - Primary cough headache
  - Primary exercise headache
  - Hypnic headache etc…..

SECONDARY HEADACHE

- Exacerbation of preexisting medical condition
  - IIH
- Initial manifestation of primary central nervous system related problem –
  - ICH with AVM
- Neurological problem unique to pregnancy and the postpartum period
  - PRES with preeclampsia

RED FLAGS

- Systemic symptoms and signs
- Neurological symptoms and signs (1 hour)
- Onset – sudden (thunderclap)
- Old age – above 50
- Pattern change/ Progression
- Precipitated by Valsalva Maneuver
- Position aggravation
- Papilledema
- Gestational age, Third trimester
- Abnormal labs: abnormal liver enzymes, elevated creatinine, platelet abnormalities

MIGRAINE DIAGNOSTIC CRITERIA AND EPIDEMIOLOGY

Migraine without aura ICHD3, 2018

- 80% females with migraine experience the attacks
- About 60% improves after 1st trimester
- Migraine with Aura less likely to improve
- Migraine with or without aura can be first symptoms during pregnancy

Robbins MS et al. Neurology. 2015 Sep 22;85(12):1024-30
Negro et al. J Headache pain, 2017;18(1):106.
Sances G, Granella F et al Cephalalgia. 2003 Apr;23(3):197-205,
Granella F, Sances G et al. Cephalalgia. 2000 Oct;20(8):701-7
Granella F, Sances G et al Headache. 1993 Jul-Aug;33(7):385-9

THE FACTS

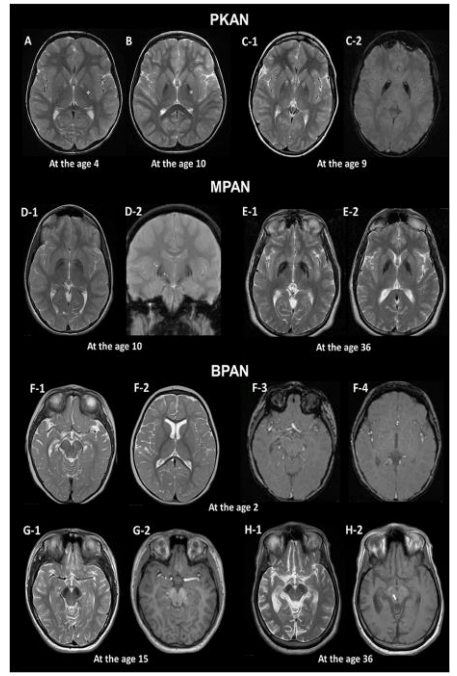
- **Association of Migraine (maternal)**
  - Cerebrovascular events (6.8-8 times)
  - Pre-eclampsia & Hypertensive disorders with aura (1.4- times)
  - Hypercoagulable disorders including central venous sinus thrombosis

- **Association of Migraine (fetal)**
  - low birth weight (1.1-1.8 times)
  - Preterm birth (1.2-1.7 times)
  - Spontaneous abortion possibly

- **Monitor for complications**

Purdue-Smithe AC et al. Neurology. 2023 Apr 4;100(14):e1464-e1473. Skajaa N et al. Headache. 2019 Jun;59(6):869-879.
Crowe HM et al. J Headache Pain. 2022 Dec 20;23(1):162. Miller EC et al. Am J Obstet Gynecol. 2022 Sep;227(3):535-536

IMAGING RECOMMENDATION AND GUIDELINES (ACOG AND ACR)



Brain Tumor Imaging for Diagnosis and Surveillance

- Non- contrast MRI is best modality (less than 3T magnet)
- Use of Gadolinium when maternal benefit outweighs risk to fetus
- CT head contraindicated d/t ionizing radiation (only for emergency stroke or hemorrhage)
- Shielding of uterus
- Intrauterine exposure is about 1/3rd of maternal exposure
- Per guideline limit exposure to 50 mGy
- Cumulative exposure at or above 150 mGy – high risk for congenital malformation and 3% lifetime risk for cancer

CASE 1

PRECONCEPTION COUNSELLING

Ishii et al Mayo Clin Proc 2020 95, 1079-1089

30 years old woman with history of migraine without aura

- Migraine frequency 6 days/month, well-controlled on Sumatriptan rescue

20 % women avoid pregnancy due to fear

Maximize nonpharmacological lifestyle recommendations

Sleep regular hours, avoid naps
Consume 4-6 portions daily
Exercise regularly
Hydrate 64-128 ounces daily
minimize caffeine
Avoid triggers
Maintain work schedule

CASE 2 RESCUE TREATMETN

JP is 30 years old female with G2P1 who is 16 weeks of pregnant
No improvement of improvement after 1st trimester
Frequency 1-2/week , associated with nausea
Use of Rizatriptan prior to pregnancy, but has not used since pregnant

First- line	Second-line	Avoid	Contraindication
Acetaminophen	Triptans	Indomethacin	Ergots
NSAIDS (12-20weeks)	ASA 81	Opiates	Gepants
Metoclopramide	Ondansetron		Lasmiditan
Diphenhydramine	Prochlorperazine		
Lidocaine	Promethazine		
Caffeine	Prednisone		
Neuromodulation??	Butalbital		

Peretz A et al. Headache. 2023 Jul-Aug;63(7):968-970.

Burch R, Epidemiology and Treatment of Menstrual Migraine and Migraine During Pregnancy and Lactation: A Narrative Review. Headache. 2019, and updated as of Jan 2024

CONTROVERSIES

Triptans

- Comprehensive literature regarding safety (Post-marketing registry study, national registry database studies, case control study, other cohort studies)
- Not associated with increased risk of major congenital malformations or spontaneous abortion
- Avoid use in hypertensive disorders, IUGR, placental insufficiency

Ephross and Sinclair, Headache. Jul-Aug 2014;54(7):1158-72

Spielmann K et al. Cephalalgia. 2018 May;38(6):1081-1092.

Roberto G et al. Cephalalgia. 2014 Jan;34(1):5-13

Butalbital

- Increase risk of cardiac malformation

Viard D et al. Eur J Clin Pharmacol. 2020 Sep 4.

Acetaminophen

- association with autism, ADHD, language delay in girls
- duration of use, higher doses
- recommend using only when needed

Bauer, A.Z., Swan, S.H., Kriebel, D. *et al.* Paracetamol use during pregnancy — a call for precautionary action. *Nat Rev Endocrinol* **17**, 757–766 (2021). https://doi.org/10.1038/s41574-021-00553-7

LOCAL INJECTION THERAPY AND OTHERS

- Occipital nerve blocks/ Trigger point injection

  SC lidocaine has good evidence for safety

  May also be used monthly or quarterly as preventive strategy
- Cyproheptadine
- Steroids
- Limited oral opioids (avoid parenteral)
- Cyclobenzaprine
- NSAIDs if in 2nd trimester

PREVENTIVE TREATMENT

Table 2. Interventions for Prevention of Headaches in Pregnancy*

Drug or Therapy	Class	Recommendation	Potential Associated Risks
Amlodipine[1,2]	Calcium channel blocker	Consider as first line use for prevention	None
Cyproheptadine[1]	Antihistamine	Consider as first line use for prevention	None
Diphenhydramine[1]	Antihistamine	Consider as first line use for prevention	None
Nifedipine[1,2]	Calcium channel blocker	Consider as first line use for prevention	None
Verapamil[1,2]	Calcium channel blocker	Consider as first line use for prevention	None

ACOG
The American College of Obstetricians and Gynecologists

Headaches in Pregnancy and Postpartum

UPDATES OF PREVENTIVE MEDICATIONS

First line	Second line	Third line	Avoid when possible	Contraindicated
Nifedipine	Propranolol	Gabapentin	Candesartan	Topiramate
Verapamil	Amitriptyline	Pregabalin	CGRP monoclonal Antibodies	Valporic acid
	Nortriptyline	Riboflavin	Gepants	Methergine
	Cyclobenzaprine	Magnesium	Venlaflaxine	Feverfew
	Cyproheptadine		Lisinopril	

Onabotulinum toxin A considered as second/third line

Safety of herbs and supplements not studied

Burch R, Epidemiology and Treatment of Menstrual Migraine and Migraine During Pregnancy and Lactation: A Narrative Review. Headache. 2019 Oct 3; updated as of Jan 2024

ONABOTULINUM TOXIN

First case during pregnancy in 1996

Almost certain does not cross placenta

POLO JM ET AL. LANCET. 1996 JUL 20;348(9021):195

500 cases of onabotulinum toxin A use during pregnancy have been reported

- Recent cumulative update from Allergan safety database (29 years of data)

- 397 eligible pregnancies
- 30% for migraine; 35% aesthetic
- 95% prior to conception or in the first trimester
- No increased signal of safety problems

Brin MF et al. Neurology. 2023 Jul 11;101(2):e103-e113.

Case series of ~55 patients treated with onabotulinum toxin A for chronic migraine throughout pregnancy

- Live full-term births of healthy babies with no organ malformations

- Summers JE et al. Safety of using onabotulinumtoxinA for the treatment of chronic migraine in pregnancy. Presented at: Virtual Annual Scientific Meeting; AHS

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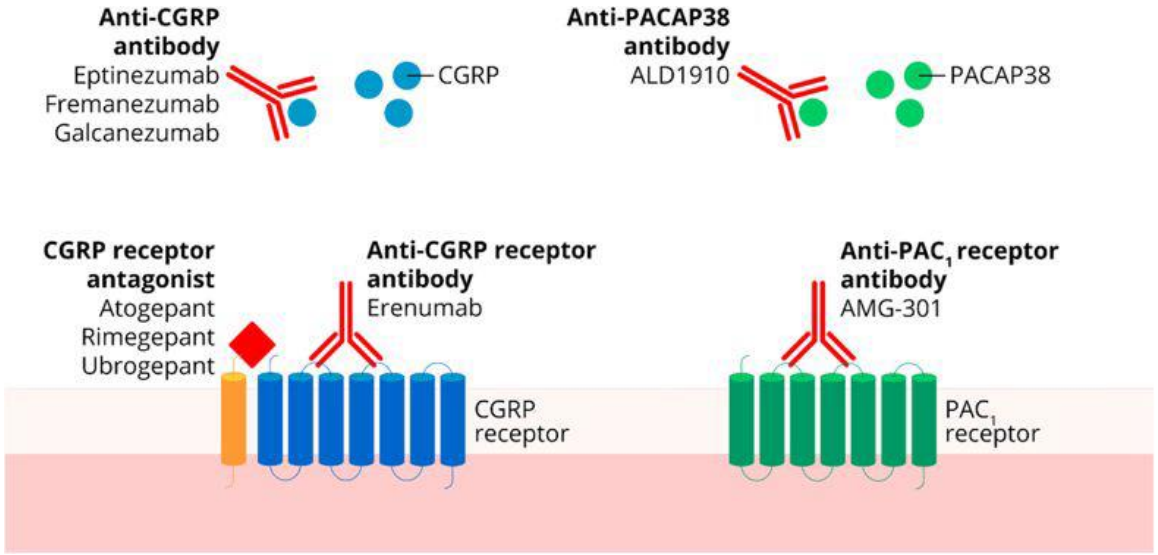
TAKE HOME MESSAGES

- Most of patients do not continue Onabotulinum treatment during pregnancy
  - Reassuring data, but cannot be conclusive
- Systemic spread after local injection
- Improvement in migraine symptoms
- Dose and Duration of treatment
- Risk versus benefit
- Discuss with patients and Document well

CGRP ANTAGONIST



Do, T.P., Guo, S. & Ashina, M. Therapeutic novelties in migraine: new drugs, new hope? J Headache Pain (2019) 20: 37.

- Participates in placental implantation and cell differentiation
- Placental vessel relaxation
- Inadequate response to CGRP – in development of pre-eclampsia
- WHO (Vigibase) database- no increase reporting of safety events compared to Triptans
- Bottom line- no strong date- DO NOT USE

Chauhan M et al.
Endocrinology. 2022 Jan 1;163(1):bqab204

Yallampalli C et al. Curr Vasc Pharmacol. 2013 Sep;11(5):641-54.

Dong YL et al. J Clin Endocrinol Metab.
2005 Apr;90(4):2336-43.

SUPPLEMENTS AND HERBS

Magnesium

- IV more than 5 days
- ACOG (risks vs benefits)
- Not first line
- Continue for those already on

CO Q10

- 200mg daily
- Second half
- No adverse fetal outcomes

Riboflavin

- Safety at higher does not established

Feverfew

Butterbur

- Contraindicated
- Increase abortion

SECONDARY HEADACHE : PREGNANCY SPECIFIC CONSIDERATION

- Preeclampsia/ eclampsia
- Cerebrovascular accident (ischemic or Hemorrhagic)
- Reversible Cerebral Vasoconstriction Syndrome (RCVS)
- Cerebral venous sinus thrombosis
- Idiopathic Intracranial Hypertension
- Pituitary Apoplexy
- Post spinal tap headache
- Chiari Malformation
- Intracranial tumor

CASE 3

36 years old G1P0 women who is 34 weeks pregnant presented with new onset headache and intermittent blurring of vision for last 1 week. She has been using over the counter medication (Acetaminophen) 3-4 times a day without any relief.

Exam- vitals HR 70/min, BP 162/110, RR-18/min, afebrile

No neurological deficits

HYPERTENSIVE DISORDERS OF PREGNANCY ACOG 2013

- Chronic Hypertension
- Preeclampsia (with or without severe features)
- Superimposed Preeclampsia
- Gestational Hypertension
- Eclampsia
- HELPP Syndrome

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PREECLAMPSIA DIAGNOSTIC CRITERIA

BLOOD PRESSURE

≥ 140 mm Hg systolic or ≥ to 90 mm Hg diastolic on two occasions at least 4 hours apart at 20 weeks' gestation

≥ 160 mm Hg systolic or ≥ 110 mm Hg diastolic; hypertension can be confirmed within a short interval (minutes)

AND

PROTEINURIA

> 300 mg per 24-hour urine collection *OR* protein-creatinine ratio > 0.3 mg/dL

Dipstick reading of 1+ (used only if other methods are not available)

OR in the absence of proteinuria, new-onset of any of the following:

Severe Symptoms

Thrombocytopenia	Platelet count < 100,000/mm^3
Renal insufficiency	Serum creatinine concentrations > 1.1 mg/dL or a doubling of serum creatinine
Impaired liver function	Elevated serum concentrations of liver transaminases to twice normal levels
Pulmonary edema	
Cerebral or visual symptoms	

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HYPERTENSIVE DISORDERS

Chronic Hypertension

- Hypertension prior to pregnancy or prior to 20 weeks of gestational age
- Hypertension after 20 weeks of gestational age but persists 12 weeks post partum
- Medication optimization

Superimposed Preeclempsia

- New proteinuria in chronic hypertensive patients after 20 weeks of gestational age
- Sudden increase in protein, pressures, other findings in patient with nephrotic syndrome and hypertension prior to 20 weeks

HYPERTENSIVE DISORDERS

Gestational hypertension

- Not preeclampsia
- BP ≥ 140/90 mm Hg
- 10% eclamptic patients with seizures but no proteinuria
- May associated with poor outcome

HELLP syndrome

- Hemolysis
- Elevated liver enzymes
- Low platelets

EPIDEMIOLOGY

- Prevalence 4.6% pregnancy worldwide, 3.4% in USA
- Prevalence increases near the term (2.7% after 34 weeks, 0.3% before 34 weeks) and up to 23 days postpartum, can be up to 6 weeks
- Clinical features: Headache, vision changes, weight gain, swelling, nausea, shortness of breath, right upper quadrant pain
- Risk factors

Risk factor	Relative risk
Prior Preeclampsia	8.4
Chronic hypertension	5.1
Pregestational DM	3.7
Multi-gestational pregnancy	2.9
FH of preeclampsia	2.9
History of Auto-immune disease	1.8-2.8
Obesity BMI >30	2.8
First pregnancy	2.1
Chronic renal failure	1.8

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COMPLICATIONS

Short term maternal complication

- PRES Posterior Reversible Leukoencephalopathy Syndrome
- Stroke, 36% of stroke in pregnancy due to eclampsia/preeclampsia
- Liver hemorrhage or rupture
- Acute Pancreatitis

Fetal complications

- Growth restriction
- Preterm delivery
- Placental abruption
- Fetal loss

MANAGEMENT

Depends on gestational age

Definite treatment is delivery of fetus, decrease maternal and fetal complications

Deliver the fetus-

- Preeclampsia with severe features, GA ≥ 34 weeks
- Previable gestational age
- Fetus or mother status not stable

If GA< 34 weeks and fetus and mother stable

- Antenatal steroids Dexamethasone
- BP control
- Magnesium
- If severe features, deliver at 34 weeks
- Without severe features deliver at 37 weeks

Hypitat trial 30% reduction in maternal mortality and morbidity

BP MANAGEMENT

- Acute setting
  - Hydralazine – 5-10 mg q15-20 mins
  - Labetalol- 20 mg iv; 40 mg iv 10 mins, 80mg iv 10 mins; not more than 220mg in a single episode (chronic)
  - Nifedipine 10 mg oral, repeat in 30 minutes; SL hypotension (chronic)

ECLAMPSIA – LIGHTENING STRIKE

- Bossier du Sauvages
- Prevalence- 1 in 200– 3500 pregnancy
- GTC in pregnancy in the absence of seizure disorder
- No predictors for patients who will develop seizure
- Headache most common symptom

MANAGEMENT

- Magnesium
- Intramuscular in 1900
- Intravenous 1920
- MgSO4-
  - 6 gm load and 2 gm iv or 5 gm im buttock
- Randomized control trials in 1990 demonstrated superiority
- NNT – 60
- Keppra for seizure prevention under investigation

RESOLUTION OF SYMPTOMS

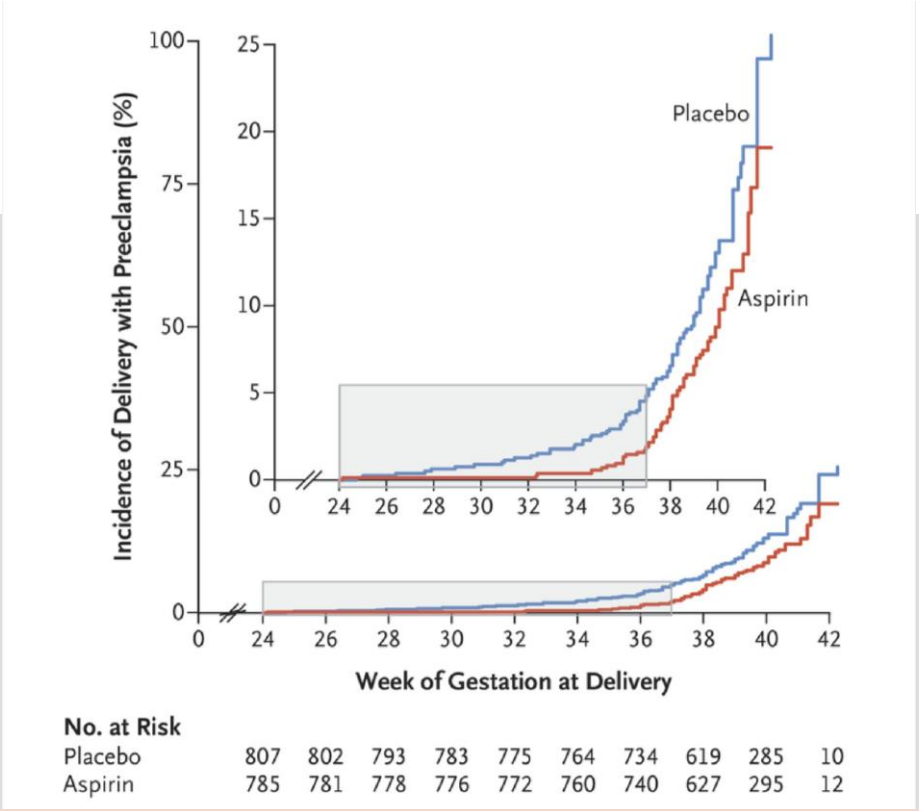
- Postpartum HTN worsen in 1-2 weeks and normalize in 4 weeks
- Resolution of Headache in hours
- Resolution of proteinuria- weeks
- Swelling – 48 hours

PREVENTION

ASA low dose, by 16 weeks

Decrease 10-20% preeclampsia in mod- high risk pregnancy

2019 Cochrane metanalysis



Preterm preeclampsia occurred in 13 of 798 participants (1.6%) in the aspirin group, as compared with 35 of 822 (4.3%) in the placebo group (adjusted odds ratio in the aspirin group, 0.38; 95% confidence interval, 0.20 to 0.74; P=0.004)

Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia. NEJM, 2017. Daniel L. Rolnik, M.D et al.

LIFELONG RISKS

Gestational age at delivery and severity also determines the lifelong risks

Mild	RR 2.0
Moderate	RR 3.0
Severe	RR 5.3

Lifetime intervention decrease risk from 4-13%

Disease	Lifetime risks
Hypertension	3.7
Ischemic Heart disease	2.2
Stroke	1.8
Venous Thromboembolic events	1.8

Schwartz et al Ana J Med 2010

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BREASTFEEDING

Observation cohort nurses` health study 2

- Never or curtailed lactation was associated with increased risk of HTN compared to > 6 months of exclusive and >12 months of total lactation per child

Nurses health study

- 23 % reduction in cardiovascular risks for women BF 2+ years in lifetime

Risk of Lifetime DM 2 increase when term pregnancy is followed by < 1 month of BF

No BF more likely to develop DM2 compared to nullipara and those with BF 1-3 months

Lactmed site

No need for pump and dump with contrast

Can pump prior contrast or medication dosing

- Staube Ob/Gyn 2009
- Staube AM J EPI 2011
- Kaiser women in California

CASE 4

- 22 year old female presented as G3P3L3, 5 days after normal vaginal childbirth with bitemporal headaches. Vitals BP- 107/77 Pulse-83. D2 hospitalization, she developed right hemiparesis; motor strength 4/5

Pregnancy-associated stroke

- Ischemic, hemorrhagic, CVST, PRES
- 50% in postpartum, 40% in 3rd trimester
- Incidence: 11-34/100,000 = 3X
- RF: peripartum infection

RISK FACTORS LEADING TO STROKES

Pregnancy related factors

- **Hypertensive disorders of pregnancy**
- Reversible Cerebral Vasoconstriction Syndrome (RCVS) / Postpartum Cerebral Angiopathy
- Cerebral Venous Sinus thrombosis
- Hypercoagulable state
- Peripartum Cardiomyopathy
- Amniotic fluid embolism
- Gestational trophoblastic disease

Non-pregnancy related factors

- Age more than 35 years
- African American
- Migraine with Aura
- Hypertension / Heart disease
- History of smoking & substance abuse
- History of Inherited thrombophilia
- History of Antiphospholipid Syndrome
- Arterial dissection / atherosclerotic disease

Physiologic changes of pregnancy can lead to higher risk of stroke

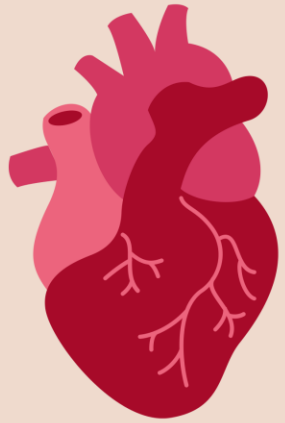
Hypercoagulable state
Venous stasis

Insulin resistance

Water retention

Increase lipids

Vascular remodeling and decreased distensibility



Increased cardiac output

SPECIAL CONSIDERATION

Gestational DM

- Is associated with stroke
- 7 times higher risk to develop DM in later life
- Early subclinical atherosclerosis and cardiovascular disease
- Increased risk of gestational hypertensive disorder

Migraine with Aura

- Higher risks of Preeclampsia → CVA
- Migraine with aura + Oral Contraceptive use – Odd ratio 7.1
- Migraine with aura + smoking – Odd ratio 9.03
- Other co-morbidities : cervical artery dissection, increase PFO prevalence, hypercoagulable/inflammatory state

SUSPECTING STROKE / STROKE ACTIVATION

- History – symptom onset, last seen normal
- Vital signs
- Serum Glucose
- CT Head and CT Angio Head and Neck
- MRI Brain
- Cardiac monitoring
- Work up for hypercoagulable states

MANAGEMENT OF ISCHEMIC STROKE

Candidate for reperfusion therapy TPA

Candidate for thrombectomy

Blood pressure management – with and without preeclampsia

Single or dual antiplatelet therapy

Best method and timing of delivery- multidisciplinary discussion with involvement of stroke expert

INTRACRANIAL HEMORRHAGE

- Arteriovenous Malformation
- Aneurysm
- Cavernous Malformation
- Moyamoya disease
- Trauma

Most commonly due to Hypertensive Disorders of Pregnancy (55%),

60 % postpartum period

Secondary to RCVS

Mortality is high, 50%

Method of Delivery – C Section/ routine, regional anesthesia (multidisciplinary approach)

Bateman BT et al Neurology 2006; 67: 424-429
Dias et al Neurosurgery 1990, 27: 855-865
Kim Y et al Neurosurgery 2013; 72: 143-149
Gross and Du et al, Journal Neurosurgery 2017; 126 : 1079-1087
Gross and Du et al Jour clin Neurosurgery 2013; 20: 44-48
Church et al Neurosurgery 2019; 134 :10-16

CEREBRAL VENOUS SINUS THROMBOSIS

AHA 2024 guidelines

- Incidence 1/2500-10000
- Common during postpartum and puerperium period
- Higher risk after delivery, infection, and hypertension
- Clinical features : Headache, seizures, encephalopathy, focal deficits, blurring of vision (papilledema)

Diagnosis- MRI Brain/MRV (TIME OF FLIGHT)

Management : LMWH throughout the pregnancy

- Postpartum LMWH or Vit K Antagonist INR 2-3 for at least 6 weeks

Future pregnancy is not contraindication

- Prophylaxis with LMWH during pregnancy and postpartum period

REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

Postpartum Angiopathy

Hypertensive disorders of Pregnancy → disrupted cerebrovascular autoregulation

Thunderclap headache is common presentation, SAH, ICH

Usually self limiting

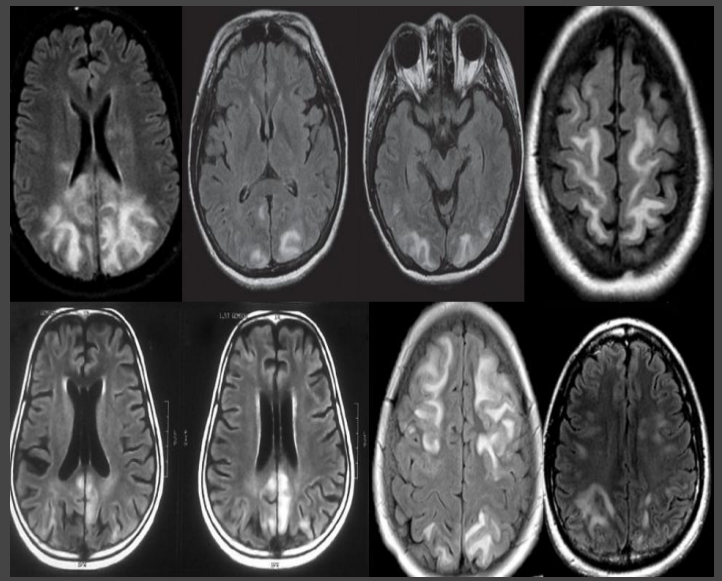
SSRI use

MRA

Delivery

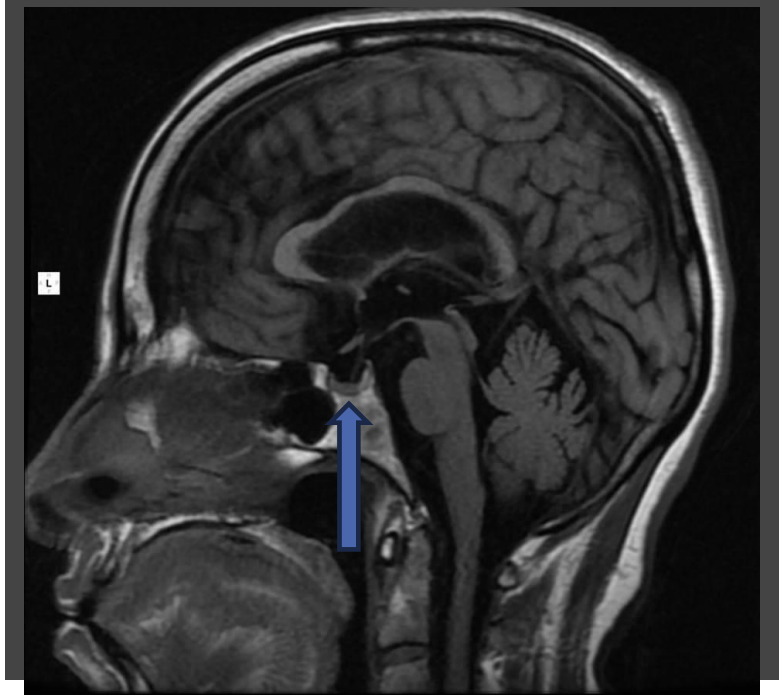
Mortality 14 %

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME



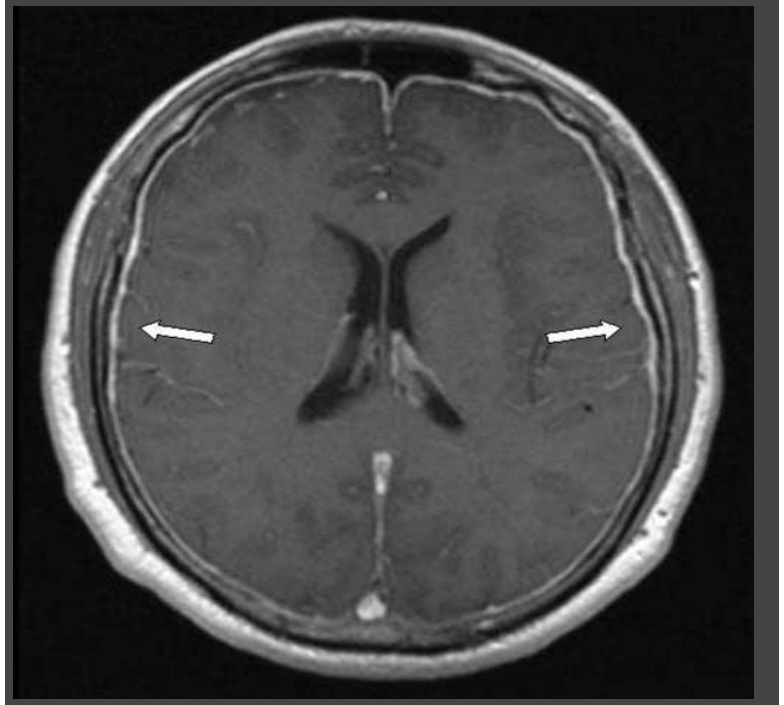
- Hypertensive disorders of pregnancy, RCVS
- Loss of cerebral autoregulation
- C/F: uncontrolled BP, headaches, seizures, blurred vision
- MRI: Gold standard
- Mx: discontinue offenders, Lower BP, treat seizures
- Deliver the fetus
- Mechanical ventilation: $PaCO_2$: 30-32 mmHg
- Vasopressors: Norepinephrine and the Phenylephrine

IDIOPATHIC INTRACRANIAL HYPERTENSION



- Idiopathic
- Previous history of IIH
- Outcomes are not different in nonpregnant women
- Mild papilledema- monitor (if no vision loss, no/minimal headache)
- Restricted weight gain (salt restriction diet)
- Acetazolamide- 2nd trimester (Cat C), Topamax (Cat D, oral clefts)
- Headache – mange headache if no vision loss
- LP
- Optic nerve sheath fenestration/ shunt
- Uterine contraction, Valsalva – increase ICP in pregnancy 3.4 cm H2O, 10.8 cm H2O without IIH; labor 70 cm H2O

POST DURAL PUNCTURE HEADACHE



- Onset 24-48 hours dural puncture but may be 5 days
- Postural nature of HA, occurring within 15 mins of standing and resolution within 15 minutes of laying down
- Conservative-Bed rest, hydration, analgesics; caffeine not supported by literature
- Epidural blood patch- lower than puncture site
- Effectiveness after 24 hours of dural puncture
- First patch – instant relief 70-97%; second patch rarely needed
- If no improvement after 2 patches, Neuroimaging should be considered
- Rare Subdural hematoma- tearing and leaking of bridging veins across subdural space, can be life threatening
- C/I to patch- Sepsis, cellulitis at the site and coagulation abnormalities

MY INSPIRATION

THANK YOU