AGA Clinical Practice Update on Diagnosis and Management of Acute Hepatic Porphyrias: Expert Review

By Cynthia Tran, MD

Diagnosis

Best Practice Advice 1:
Screening for Acute Hepatic Porphyria (AHP):
- **Women aged 15-50** w/ recurrent severe **abdominal pain without clear etiology** after an initial workup (e.g. labs, imaging, endoscopy)
- Other symptoms: ↑HR, HTN, N/V, constipation, muscle weakness, neuropathy

Best Practice Advice 2:
Initial Diagnosis of AHP, biochemical testing:
- Random **urine** sample with elevated **delta-aminolevulinic acid (ALA)** ***AND*** **porphobilinogen** - normalize to creatinine
- Levels often **>5x upper limit of normal**
- If only ALA elevated, DDx: lead poisoning vs hereditary tyrosinemia

Best Practice Advice 3:
Confirm Diagnosis of AHP, genetic testing:
- Sequencing of **4 genes**:
- *HMBS* – Acute Intermittent Porphyria
- *CPOX* – Hereditary Coproporphyria
- *PPOX* – Variegate Porphyria
- *ALAD* – 5-Aminolevulinic Acid Dehydratase Deficiency Porphyria

Acute Management & Prevention

Best Practice Advice 4:
Treatment of Acute, Severe AHP Requiring Admission:
- **Hemin 3-4 mg/kg IV daily x4 days** per central IV/port: decreases accumulation of ALA + PBG
- **Symptom relief** depends on elimination of ALA + PBG: typically requires **48-72 hrs** (neurologic recovery variable)
- Collect ALA, PBG, Cr prior to initiating tx

Best Practice Advice 5:
Treatment of Acute, Severe AHP Requiring Admission:
- Pain control, antiemetics
- Tx HTN/tachycardia
- Tx hypo-Na, hypo-Mg
- **Stop meds** that **induce Cyp450**
- **Cautious seizure management**: MgSO4, Benzos, Levetiracetam – safe meds

Best Practice Advice 6:
Prevention, precipitants/triggers to **AVOID:**
- Sex hormones, esp. Progesterone
- **Meds** that induce Cyp450
- Acute **illness/infection**
- Physical/psychological **stress**
- Excess **EtOH**
- **Tobacco** use
- **Caloric deprivation**

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Acute Management & Prevention - continued

Best Practice Advice 7:
Treatment for patients **with recurrent attacks (≥ 4 attacks per year):**
- **Givosiran**: RNA-based tx & decreases ALA + PBG production, monthly SC injection
  - Monitor: CMP, homocysteine, amylase, lipase
  - **Avoid in pregnancy/pre-pregnancy**
- Off-label **ppx Hemin**, risks: need for indwelling central access, infections, iron overload

Long-term Considerations

Best Practice Advice 8:
Limit liver transplantation to patients with **AHP refractory to pharmacotherapy** with intractable symptoms and significantly decreased quality of life:
- Liver txp restores normal ALA + PBG levels
- If living donor txp: **genetic testing to screen related living donors**

Best Practice Advice 9:
Monitor annually for liver disease:
- If ↑LFTs: also consider alternative Dx
- If receiving monthly ppx **Hemin: ferritin + iron every 3-6 mos**
- If receiving monthly **Givosiran: LFTs monthly x3-6 months then 2x/yr**

Best Practice Advice 10:
HCC Surveillance at age **50 yrs** w/ **US + AFP every 6-mos** (AASLD 2023):
- AHP → ↑**risk of HCC and CCA**
  - Poss. absence of cirrhosis/fibrosis
  - ↑Risk for symptomatic pts, but also reported in asymptomatic pts

Best Practice Advice 11:
CKD Surveillance annually w/ Cr + eGFR:
- AHP → ↑**risk of CKD and HTN**
  - Porphyria-assoc kidney disease
- Givosiran: poss. ↓ renal function
- If ESRD due to AHP: renal txp ideal as ALA + PBG levels ↑↑↑ between dialysis

Best Practice Advice 12:
Counsel patients on long-term complications: neuropathy, CKD, HTN, HCC, and need for long-term management/monitoring

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