Advanced, Organ-Based and Clinical Sciences

Acute Intermittent Porphyria (AIP) is a genetic syndrome resulting in impaired synthesis of heme (best known as an important component of hemoglobin which carries oxygen in the blood). Specifically, there is a mutation of porphobilinogen deaminase resulting in decreased activity and an accumulation of porphobilinogen. Although not well defined, the build-up of porphobilinogen is thought to be toxic to neurons, which explains the clinical presentation of effects on the peripheral and autonomic nervous systems. Classic signs and symptoms include abdominal pain, nausea/vomiting and constipation, tachycardia, dark red urine, and sometimes schizophrenic-like psychiatric effects as well as back and leg pain that may progress to paresis.

Attacks are episodic and typically triggered by inciting factors such as medications, drastic diets/fasting, or stress such as an infection or surgery.

Most notably in the practice of anesthesia, barbiturates and other CYP inducers can trigger AIP attacks. Barbiturates lead to increased levels of porphyrin by stimulating aminolevulinic acid (ALA) synthetase. These intermediaries in the heme synthesis pathway then build-up and precipitate an attack. Glucose acts to suppress ALA synthetase and thus is useful in prevention and treatment. Other known triggers include diazepam, sulfonamides, griseofulvin, sex hormones e.g. in contraceptives, glucocorticoids, phenytoin, cigarette smoke, and anti-retrovirals used to treat HIV.

Other common anesthetic agents such as propofol and fentanyl appear to be safe in this population, as do etomidate and ketamine although the latter are potential triggers in animal studies.

Although autosomal dominant, most patients have no family history of the disease as acute attacks only occur in about 10% of carriers, most commonly affecting young adult women.

Sources

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[PubMed: 29306617]

Anaesthesia. 1993 May;48(5):417-21

Porphyria: anesthesia risks

Porphyrias are a set of autosomally inherited metabolic disorders that are the result various defects in heme synthesis. Broadly, they can be classified into inducible, and non-inducible forms.

Inducible porphyrias (i.e. Acute Intermittent Porphyria) can present with acute neurological and/or GI symptoms. Patients may have anxiety, confusion, autonomic instability (manifested as hypertension or tachycardia), emesis, and severe abdominal pain. Acute attacks can be precipitated by stress, fasting, dehydration, sepsis, and certain medications, including some meds commonly used in the perioperative period.

- **Triggering agents include: barbiturates, diazepam, ketorolac, phenytoin, birth control pills and sulfonamides.**
- Drugs that are safe to use in the perioperative period include succinylcholine, atropine, neostigmine, pancuronium, nitrous oxide, procaine, meperidine, fentanyl and morphine.
- Local anesthetics are believed to be safe, but some practitioners avoid regional anesthesia in these patients, as it may be difficult to distinguish neurological complications of a regional procedure from sequelae of an acute attack.
- Although ketamine and etomidate have been used safely in patients with AIP, they have been found to be porphyrogenic in rats. Some practitioners avoid ketamine use altogether in these patients, as it can be difficult to distinguish psychoses associated with an inducible porphyria from those associated with ketamine use in some patients.

Noninducible porphyrias (i.e. Porphyria Cutanea Tarda) are not affected by drugs. They usually appear as photosensitivity reactions in males >35 years of age. These patients often have friable skin, so it becomes important to pay close attention to pressure points in the operating room environment. Practitioners should avoid excess pressure/irritation to

exposed areas (i.e. with mask ventilation or securing ETT and protecting eyes with tape, etc.). Of note, non-inducible porphyrias do not cause neurologic sequelae.