Real-World Analysis of Symptoms, Diagnostic Patterns, and Provider Perspective on Acute Hepatic Porphyrias

Background and Rationale

Acute Hepatic Porphyrias (AHPs) are a group of rare, genetic diseases caused by deficient activity in one of the eight enzymes involved in heme biosynthesis (Figure 1); acute intermittent porphyria (AIP) is the most common subtype. Accumulation of neurotoxic heme intermediates, urinary aminolevulinic acid (ALA) and porphobilinogen (PBG), can cause chronic debilitating symptoms and potentially life-threatening attacks. First-line diagnostic biochemical tests include measuring urinary ALA and PBG as both are elevated in the majority of AHPs; conversely, testing urinary porphyrins, alone, is less specific as elevations are observed in other more common disorders. Low awareness of optimal diagnostic tests leads to a delay in diagnosis.

Methods

Methodology

- Health Care Providers (HCPs) (N=175) from the US, EU, Canada, Japan, and Korea who had actively managed or treated patients were included.

Participants were recruited between September 15 to October 10, 2017 (until November 30th in Japan and EU).

- HCPs were included if they met the following criteria:
  - Board certified or eligible
  - Practice experience of 2-35 years
  - Can provide at least one patient chart
  - Active provider of the primary care provider for at least 1 AHP patient

- HCPs completed an online survey collecting information on demographics, familiarly with AHPs and diagnostic tests, perspective on symptoms important to diagnosis, referral patterns, and treatment preferences.

- HCPs were asked to provide 1-4 AHP patient charts; chart data included anonymized patient demographics, medical history, number of porphyria attacks, and symptoms.

Results

HCP Demographics

- Mean of 18.1 years in practice
- HCPs were actively managing a median of 8 AHP patients (mean 21.3, SD 32.6) and have seen a median of 16 AHP patients in the past year (mean 40.3, SD 14.2)

- HCP practice setting was community setting/primary care (47%), private practice (20%), group practice (17%), academic medical center (7%), and teaching hospital (5%) (Figure 2a).

- HCPs are engaged in various subspecialties (Figure 2b).

- On average 3 AHP patient charts were provided per physician for a total of 546 charts (32% US) (Table 1).

- HCPs reported symptoms considered informative for AHP diagnosis, including abdominal pain, red/dark urine, muscle weakness, vomiting, fatigue, and nausea (Figure 3).

- AHP diagnostic tests considered informative included ALA in urine and PBG in urine; however, other nonspecific tests were also commonly considered informative (e.g., porphyrin in the urine) (Figure 3).

Symptoms and Diagnostic Tests Considered Informative to AHP Diagnosis

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Chart Review: Patient Demographics

- 546 total AHP patient charts were abstracted
- Majority of patients were diagnosed with AIP; mean patient age was 40.3 years, slightly more patients were female (Table 2)

- According to patients’ HCPs, the majority of patients were employed at some level (60%); however, over a quarter were unemployed or disabled (27%).

- Females reported more abdominal pain and anxiety; males reported more muscle weakness, fatigue, and nausea (Table 2).

- Employment status was divided into full-time, part-time, unemployed, retired, or disabled (Table 2).

Chart Review: Patient Misdiagnosis

- 26% of AHP patients were initially misdiagnosed and 31% were diagnosed correctly (43% did not know this information) (Figure 4a).

- Most common misdiagnoses reported were nonspecific abdominal pain, irritable bowel syndrome (IBS), depression, and fibromyalgia (Figure 4b).

Factors Affecting Patient Severity

- Impact on quality of life, acute neurologic symptoms, acute abdominal pain, chronic neurologic symptoms, and chronic abdominal pain are considered important for HCP assessment of AHP severity (Figure 5).

Summary

- Data supports that AHPs are often underdiagnosed or misdiagnosed likely due to nonspecific symptomology and/or lack of understanding of optimal laboratory testing procedure.

- AHPs have both acute and chronic manifestations impacting patient’s quality of life; these symptoms play an important role in the diagnosis and assessment of severity amongst AHP patients.

- Limitations include potential retrospective selection bias from HCPs pulling charts of their most severe patients and the greater proportion of males than cited in literature, limiting generalizability of results.

References:


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