Molecular Genetics and Metabolism 119 (2016) 278–283

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism

journal homepage: www.elsevier.com/locate/ymgme

# Experiences and concerns of patients with recurrent attacks of acute hepatic porphyria: A qualitative study

Hetanshi Naik MS *, Mikayla Stoecker MS, Saskia C. Sanderson PhD, Manisha Balwani MD, MS, Robert J. Desnick MD, PhD

*Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, NY 10029, Unites States*

ARTICLE INFO

*Article history:*
Received 13 June 2016
Received in revised form 22 August 2016
Accepted 22 August 2016
Available online 24 August 2016

*Keywords:*
Acute hepatic porphyria
Acute intermittent porphyria
Focus groups
Psychosocial experiences
Quality of life

ABSTRACT

*Background:* The acute hepatic porphyrias (AHPs) are rare inborn errors of heme biosynthesis, characterized clinically by life-threatening acute neurovisceral attacks. Patients with recurrent attacks have a decreased quality of life (QoL); however, no interactive assessment of these patients' views has been reported. We conducted guided discussions regarding specific topics, to explore patients' disease experience and its impact on their lives.
*Methods:* Sixteen AHP patients experiencing acute attacks were recruited to moderator-led online focus groups. Five groups (3–4 patients each) were conducted and thematic analyses to identify, examine, and categorize patterns in the data was performed.
*Results:* All patients identified prodromal symptoms that began days prior to acute severe pain; the most common included confusion ("brain fog"), irritability, and fatigue. Patients avoided hospitalization due to prior poor experiences with physician knowledge of AHPs or their treatment. All patients used complementary and alternative medicine treatments to avoid hospitalization or manage chronic pain and 81% reported varying degrees of effectiveness. All patients indicated their disease impacted personal relationships due to feelings of isolation and difficulty adjusting to the disease's limitations.
*Conclusion:* Patients with recurrent attacks recognize prodromal warning symptoms, attempt to avoid hospitalization, turn to alternative treatments, and have markedly impaired QoL. Counseling and individualized support is crucial for AHP patients with recurrent attacks.



## 1. Introduction

The three autosomal dominant acute hepatic porphyrias (AHPs), Acute Intermittent Porphyria (AIP), Variegate Porphyria (VP), and Hereditary Coproporphyria (HCP), are rare disorders of heme biosynthesis [1,2]. AIP is the most common with an estimated heterozygote prevalence of ~5.4 per 100,000 in Europe, and a higher frequency in Scandinavia due to a founder mutation [3]. The actual heterozygote prevalence is unknown, as it is estimated that 80–90% of heterozygotes never experience symptoms [1–3]. Symptoms are characterized by life-threatening acute neurovisceral attacks of severe abdominal pain, nausea, vomiting, and tachycardia that, if untreated, may lead to seizures, hallucinations, brain stem involvement and paralysis [1–6]. A small subset of patients experience recurrent attacks, most of whom are women [1,2,4]. While the acute attacks in the three AHPs are clinically similar, VP and HCP patients can also have blistering skin photosensitivity and are reported to have less frequent attacks [1–4].

The AHPs are diagnosed during an attack by demonstrating markedly elevated urinary and/or plasma levels of the neurotoxic porphyrin precursors, 5-aminolevulinic acid (ALA) and porphobilinogen (PBG) [6,8,9]. However, diagnosis is often delayed due to the nonspecific symptoms and lack of awareness of these rare disorders among physicians. Certain precipitating factors are known to cause acute attacks including hormonal changes, excess alcohol, fasting, and porphyrogenic medications such as those that induce P450 enzymes [1,2,7]. Stress has been described as a possible precipitating factor [7,9,10], although the extent to which stress induces acute attacks has not been described.

The current treatment for acute attacks is intravenous infusions of hemin, which is typically infused at 3–4 mg/kg for 4 consecutive days [8–11]. However, some patients with recurrent attacks receive prophylactic hemin infusions, ranging from weekly to monthly, to prevent hospitalization [10,12–14].

Previously, there have been only a few studies of the patient experience with this disease, particularly among patients with frequent recurring attacks. These studies have reported that symptomatic AHP

* Corresponding author at: Department of Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1497, New York, NY 10029, United States.
*E-mail addresses:* hetanshi.naik@mssm.edu (H. Naik), mikayla.stoecher@Swedish.org (M. Stoecker), saskia.sanderson@ucl.ac.uk (S.C. Sanderson), manisha.balwani@mssm.edu (M. Balwani), robert.desnick@mssm.edu (R.J. Desnick).

http://dx.doi.org/10.1016/j.ymgme.2016.08.006
1096-7192/

patients have decreased quality of life (QoL), an increased incidence of anxiety and depression, impaired physical functioning, and a negative disease impact on employment [15–17]. The experiences of five women over 55 years old who had recurrent acute attacks were assessed using individual structured interviews [18]. However these women were specifically selected because they were "successful in coping with their lives." Focus group studies are widely used in common diseases and public health issues, such as cancers, autoimmune diseases, and diabetes, to understand patients' perspectives. [19–21]. These have resulted in targeted outreach programs, improved marketing of screening programs, and more patient-friendly counseling methods. Some have been performed in other rare disease populations as well with good results [22–24]. Focus group methodology specifically allows patients to compare experiences and creates an environment for sharing personal experiences, feeling, and concerns which may not otherwise be brought to the attention of providers. As well, focus groups are ideal to identify gaps in care and knowledge and generate hypotheses for future studies [25,26].

Here we assessed the experiences of patients with recurrent attacks, whether they recognize prodromal symptoms of an acute attack, and their decision-making process about treatment, areas which have not been previously investigated. In addition, we sought to learn how patients manage their acute and chronic porphyric pain, and the extent to which stress can exacerbate or induce this pain. These areas represent gaps in our knowledge and understanding of the impact of the AHPs on QoL. Therefore, we conducted focus groups with the primary objective to explore patients' perspectives on their disease, as well as to examine specific topics identified by the study team to improve management and counseling of these patients.

## 2. Methods

### 2.1. Participants

The study sample was comprised of patients 18 years or older who were recruited from the Porphyrias Consortium of the NIH-sponsored Rare Diseases Clinical Research Network from October 2013 to March 2015. All patients were participating in the Longitudinal Study of the Porphyrias (NCT01561157). Twenty patients were sent an information sheet from their respective Porphyrias Consortium site inviting them to participate in this study. Seventeen expressed interest in participating, the study was reviewed with them in detail over the telephone and verbal consent was obtained. All participants had a genetically confirmed AHP diagnosis and documented elevated urine PBG levels. The Institutional Review Board at the Icahn School of Medicine at Mount Sinai approved this research. Sixteen AHP patients participated in one of five focus groups, with 3–4 participants per group, and all completed a demographic survey (Table 1). The 17th patient could not participate due to scheduling conflicts.

### 2.2. Data collection and focus group guide

Focus groups were conducted by two members of the research team and questions were specifically designed to be open-ended and unbiased to encourage discussion. Given the rarity of the AHPs and the geographic distribution of the American patients, in-person groups were not feasible. Instead, online video conferencing software GoToMeeting (www.gotomeeting.com) was used to conduct the focus groups. GoToMeeting security controls meet the Health Insurance Portability and Accountability Act (HIPAA) regulations and participants were specifically informed about this. All focus groups were audio recorded and sessions typically lasted for 1.5–2 h. Follow up interviews to further probe patient experiences and opinions on topics raised during the sessions were conducted via telephone.

A topic guide was developed based on a review of the literature regarding QoL, patient experiences, triggers that cause acute attacks [7,8–10,13–18] and expertise of the research team. The Guide consisted of five sections, each with a brief introduction followed by one to three open-ended questions (Table 2). Appropriate prompts were used during the sessions if necessary to facilitate discussion. The Guide was constructed to address participants' 1) opinions on their disease; 2) opinions of whether they have prodromal symptoms and their understanding of them; 3) experience with medical treatment; 4) opinions on if/how stress affects them; and finally, 5) methods of pain management.

**Table 1**
Characteristics of participants.

| Characteristics | Participants (n = 16) |
|---|---|
| Age, mean years (SD), range | 38 (13.6), 19–67 |
| Age at onset of symptoms, mean years (SD), range | 25 (10.3), 11–55 |
| Age at diagnosis of AHP, mean years (SD), range | 27 (11.4), 10–55 |
| Type of AHP | |
| Acute Intermittent Porphyria | 15 (94%) |
| Variegate Porphyria | 1 (6%) |
| Sex | |
| Female | 15 (94%) |
| Male | 1 (6%) |
| Ethnicity | |
| Caucasian | 15 (94%) |
| African American | 1 (6%) |
| Marital status | |
| Married | 9 (56%) |
| Single | 7 (44%) |
| Frequency of acute attacks | |
| Monthly | 10 (63%) |
| Several times per year | 6 (37%) |
| Family members who have had acute attacks | |
| Yes | 12 (75%) |
| No | 4 (25%) |
| Education level | |
| Some college | 4 (25%) |
| College graduate | 9 (56%) |
| Advanced degrees | 3 (19%) |
| Employment | |
| Full time employed | 7 (44%) |
| Part time employed | 1 (6%) |
| Unemployed due to AHP | 5 (31%) |
| Unemployed by choice | 1 (6%) |
| Student | 2 (13%) |
| Disease has prevented work in field of choice | |
| Never | 3 (19%) |
| Occasionally | 5 (31%) |
| Frequently | 4 (25%) |
| Always | 4 (25%) |

### 2.3. Data analysis

Focus group recordings were transcribed verbatim and then de-identified. Data were analyzed using thematic analysis [27]. Briefly, transcripts were manually coded and organized based on their content into categories by two authors (MS and HN) independently. New categories were created until a repeating category was identified, themes were extracted from the categories, and a codebook was developed. Differences between the two coders were identified and reconciled between the investigators.

## 3. Results

### 3.1. Participants

Of the 16 participants, 15 (14 female, 1 male) had AIP, and one female had VP. The median age was 38 years (range 19–67 years), and all had completed at least some college education, with the majority (56%) having a college degree. Fifteen participants had or were currently having recurrent attacks, defined as more than four patient-reported acute attacks a year that required treatment with hemin or increased