REVIEW ARTICLE

Anesthetic Considerations in Porphyrias

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Porphyrias present special anesthetic challenges, including preoperative assessment of a patient with acute abdominal pain, intraoperative management of known porphyria, and respiratory and cardiovascular management of acute porphyric crisis. To meet these challenges, a current and thorough understanding of porphyria is essential. Several years have elapsed since there has been a comprehensive review of the spectrum of issues related to porphyria of concern to the anesthesiologist: presentation, pathophysiology, monitoring, and relevant pharmacology. The last significant review of this subject provided a pharmacologic perspective, but much relevant anesthetic information was not addressed, such as new methods of detection and the evolving role of hematin and heme arginate in treatment (1). Deoxyribonucleic acid analysis of suspected porphyric patients promises earlier, definitive diagnosis of the disease and thereby the opportunity for safer anesthetic management. This management may soon include heme arginate, the most stable form of heme, which currently lacks approval by the Food and Drug Administration but is soon to be tested in clinical trials in the United States. Safe anesthetic management of porphyria demands far more today than an understanding of appropriate pharmacologic therapy. It demands a thorough, current understanding of many other aspects of the disease.

Pathophysiology

The porphyrias are a group of inherited or acquired enzymatic defects of heme biosynthesis. Each type of porphyria has a characteristic pattern of overproduction and accumulation of heme precursors based on the location of the dysfunctional enzyme in the heme synthetic pathway (Fig. 1)

The rate-limiting step in heme synthesis is the condensation of succinyl coenzyme A and glycine to form δ-amino levulinic acid (ALA) (2,3), catalyzed by the mitochondrial enzyme ALA synthetase. The basal activity of ALA synthetase is substantially lower than that of subsequent enzymes in the synthetic pathway, and therefore changes in ALA synthetase activity are rate-limiting, controlling the rate of heme synthesis. Heme, the end-product of the synthetic pathway, exerts negative feedback regulation on ALA synthetase activity (4–6).

The specific enzyme deficit in each type of porphyria results in a partial block in heme biosynthesis and lower intramitochondrial heme levels (Fig. 1). Decreased negative feedback from heme contributes to the increased "baseline" ALA synthetase activity which is characteristic of the porphyrias (4–6).

The manifestions of the disease are thought to be due to increased ALA synthetase activity, increased porphyrin accumulation in the tissues, or decreased heme production (4–6). The increased ALA synthetase activity results in increased levels of heme precursors proximal to the site of the specific enzyme deficiency. These precursors are colorless and nonfluorescent porphyrinogens. Irreversible oxidation of these porphyrinogens causes the formation of porphyrins, which have no known physiologic function but are highly reactive oxidants. The accumulation of porphyrins in the epidermal skin layers lead to cutaneous photosensitivity. (7)

Acute porphyria often causes severe neuropathy, the basis for multisystem impairment. Changes in autonomic ganglia, anterior horns of the spinal cord, peripheral neves, brainstem nuclei, cerebellar axons, Schwann cells, and myelin sheaths have been demonstrated (6,8–12). Neuronal damage and axonal degeneration may be the primary pathologic lesions, with later axonal changes leading to secondary demyelination (4,6).

Many hypotheses have been porposed to explain the mechanism of porphyric neuropathy (4,9). Two of the most plausible attribute the neuronal dysfunction to direct neurotoxicity of ALA (not porphobilinogen [PBG]), or to diminished intraneuronal heme level or both (4,6,11). In addition, there may be a significant relationship between tryptophan metabolites and/or

Accepted for publication August 18, 1994.

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0003-2999/95/$5.00

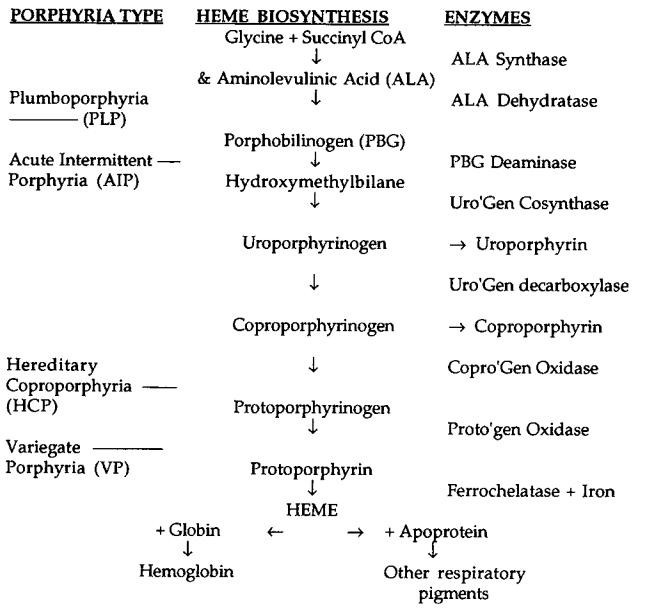

Figure 1. Enzymatic defects in the acute porphyrias. The porphyrias are a group of inherited or acquired enzymatic defects of heme biosynthesis. Each type of porphyria has a characteristic pattern of overproduction and accumulation of heme precursors based upon the location of the dysfunctional enzyme in the heme synthetic pathway. Modified from Moore et al. (4).

folate deficiency and clinical expression of the disease (13,14). Recent reviews provide additional detail (4,6,9).

Classification and Incidence

The porphyrias may be classified according to three characteristics:

1. The major site of abnormal porphyrin production (hepatic versus erythropoietic);
2. Acute or nonacute presentation;
3. Pattern of enzyme deficiency in heme production (Table 1) (4).

Heme is a component of microsomal and mitochondrial cytochrome systems and is synthesized and used in all cells. The two major quantitative sites of heme synthesis are erythropoeitic and hepatic cells where heme is incorporated into hemoglobin and hepatic cytochromes. Erythropoeitic porphyrias cause extreme skin sensitivity buy lack neurologic involvement and are not associated with drug-precipitated crises.

Porphyria cutanea tarda is the only hepatic porphyria without neurologic sequelae. Porphyria cutanea tarda is usually associated with hepatic disease but not acute neurologic crisis. Other hepatic porphyrias are associated with abdominal pain, peripheral neuropathy, and mental status changes, with crisis

Table 1. Classification of Porphyrias

Hepatic
Hepatic acute porphyrias
Acute intermittent porphyria (AIP)
Hereditary coproporphyria (HCP)
Variegate porphyria (VP)
ALA dehydratase deficiency porphyria (plumboporphyria) (PLP)
Hepatic nonacute porphyrias
Porphyria cutanea tarda (PCT)
1. Familial
2. Acquired
Erythropoietic
Erythropoietic porphyria
Uroporphyria
Protoporphyria

From Moore et al. (4).

frequently precipitated by "triggering" drugs. Barbituates are the most frequent "trigger" (9,15). There is little difference in the neurologic syndrome exhibited during an attack among the four acute hepatic porphyrias. Hereditary coproporphyria (HCP) and variegate porphyria (VP) manifest skin photosensitivity and extreme skin fragility, whereas acute intermittent porphyria (AIP) does not (4–6).

Once diagnosed, AIP is associated with a relatively good prognosis. Symptoms occur in less than one-third of genetically susceptible patients but rarely before puberty. Acute attacks are associated with a significant risk of mortality, particularly if the diagnosis is delayed and neurologic involvement progresses. Although autosomal dominant, clinical expression is more common in females (16).

Most patients with HCP are asymptomatic and clinical onset may be associated with intercurrent hepatic disease. Presentation has occurred between the ages of 7 and 75 yr. Prognosis is generally good (17).

VP has a prognosis as good as acute intermittent porphyria. Systemic effects are more common in women, while cutaneous manifestations are more common in men (17).

Treatment of known hepatic porphyria consists of prophylaxis and treatment of the acute attack.

Factors known to precipitate acute porphyric crisis include fasting/dehydration, infection, psychologic stress, physiologic hormone variation, excessive alcohol intake, and administration of specific drugs. Many drugs cause porphyric crisis (Table 2). Most do so by decreasing heme levels, thus decreasing negative feedback and thereby increasing ALA synthetase activity (4–6).

Many commonly used drugs trigger porphyric crisis by decreasing heme (2). Barbiturates induce the cytochrome P450 system; this incorporates more heme into the new cytochromes, thereby decreasing heme

Table 2. Porphyria and Anesthetic Drugs

Group	Safe-likely safe	Unsafe-likely unsafe	Unclear
Intravenous drugs			
	Midazolam	Barbiturates	Diazepam
	Lorazepam	Etomidate	Ketamine
	Propofol	Chlordiazepoxide	
		Flunitrazepam	
		Nitrazepam	
Inhaled drugs			
	Nitrous oxide	Enflurane	Isoflurane
			Halothane[a]
Neuromuscular blockers			
	Succinylcholine		Pancuronium
	Vecuronium		Atracurium
	d-Tubocurarine		
Premedicants			
	Scopolamine		
	Atropine		
	Droperidol		
	Promethazine		
	Chloral hydrate		
	Diphenhydramine		
	Cimetidine		
Opioids			
	Morphine	Pentazosine	Sufentanil
	Fentanyl		
Anticholinesterases			
	Neostigmine		
Local anesthetics			
	Bupivacaine		Lidocaine
	Procaine		
Cardiovascular			
	Atenolol	α-methyldopa	
	Labetolol	Hydralazine	
	Guanethadine	Phenoxybenzamine	
	Reserpine		
	Phentolamine		
Other			
	Glucose loading	Oral contraceptive	
	Anticonvulsants	Griseofulvin	
		Endogenous steroids	

Modified from Harrison et al. (1).
[a]Despite lack of definitive evidence of its safety, halothane is still recommended as the inhaled anesthetic of choice.

levels. Oral contraceptives cause destruction of the heme group in cytochromes, requiring new heme for incorporation into cytochromes. Griseofulvin converts heme into *N*-methylated derivatives, which further inhibit heme synthesis.

Some endogenous steroid hormones are thought to trigger porphyria by increasing the synthesis of new ALA synthetase enzyme (2). Factors known to decrease synthetase activity include high carbohydrate (glucose) loading, propranolol, and and increased negative feedback from heme (3–6,18). Propranolol is used during the acute porphyric attack to control hypertension and tachycardia. This drug increases heme synthesis *in vitro*, which exerts an inhibitory effort upon ALA synthetase activity through negative feedback (19).

The acute porphyrias are associated with hereditary enzyme deficits (20–24). AIP, HCP, and VP exhibit autosomal dominant transmission with variable expression. The frequency of AIP is estimated to be 1/20,000 in Europe, with a high of 1/10,000 in Northern Sweden (4,25). ALA dehydratase deficiency porphyria, also known as plumboporphyria (PLP), has an autosomal dominant pattern. Since PLP has been described only recently, no estimate of prevalence has been established (26–28). The frequency of HCP is also difficult to estimate since greater than half of affected individuals are asymptomatic (variable expression) and the number of reported cases is small (4). VP is particularly common in certain populations groups, such as white South Africans, where prevalence has been estimated at 1/250–500 (4,29).

Table 3. Features of the Acute Porphyric Attack

Nervous system dysfunction	Approximate Involvement (%)[a]
Autonomic neuropathy	
Abdominal pain	95
Vomiting	46
Tachycardia	80
Hypertension	36[c]
Postural Hypotension	21
Peripheral neuropathy	60
Paresis to paralysis of muscle groups or extremities	
Flaccid quadriplegia	
Respiratory paralysis	
Bulbar involvement	30
Vagal-cranial nerve	
Dysphagia	
Dysphonia	
Respiratory dysfunction	
Hypothalmic involvement	
(Syndrome of inappropriate secretion of antidiuretic hormone)	12
Pyrexia	9
Cerebral involvement: mental status changes	55[b]
Anxiety, confusion, hysteria, depression, psychosis	
Seizures	20
Coma	10
Laboratory	
Dark urine	74
Hypochloremia	50[b]
Hyponatremia	41
Hypokalemia	29[b]
siADH	12
Leukocytosis	11
Hypomagnesemia	9

[a] All data from Stein and Tschudy (35) except as noted.
[b] Percentages taken from Eales and Linder (34) due to unclear or unavailable data from Stein.
[c] Other reviews have reported values up to 55%.
Modified from Taddeini and Watson (29).

Pregnancy may exacerbate or provoke an acute attack. Avoidance of planned pregnancy until 1-yr latent period has elapsed is recommended. The mortality rate from acute attack among pregnant patients hs been reported to be as high as 42% (30).

Clinical Features: Acute Attack

Acute attacks occur in only four types of porphyria: AIP, HCP, VP, and PLP (7). The signs and symptoms of acute porphyric crisis are well known and quite consistent: severe abdominal pain, vomiting, anxiety, confusion, autonomic instability manifested by hypertension and tachycardia, dehydration and electrolyte disturbances such as hyponatremia, hypokalemia, and hypocalcemia (22,24,31) (Table 3).

AIP, HCP, and VP may be clinically indistinguishable during acute attacks (32). Central to each is neurologic dysfunction (Table 3) (9,29), with significant impairment of both sympathetic and parasympathetic nervous systems occurring during an acute attack (33). During remissions function improves but parasympathetic dysfunction can persist (33).

Tachycardia is often an indicator of disease state progression (25,34,35). As heart rate increases, the patient's condition generally worsens and with clinical improvement tachycardia usually resolves. Most of the clinical features subside within the approximate time course of the acute crises, but residual paresis may persist for years in the absence of further attacks (34). The paresis, *per se*, does not have specific implications for the use of neuromuscular relaxants. The use of muscle relaxants in the setting of porphyria is discussed below. Recovery of mental function often lags behind physical recovery, and some patients report anxiety, emotional instability, or other functional disturbances indefinitely (29).

Electrolyte abnormalities occur secondary to dehydration, vomiting, and diarrhea and may entail serious hyponatremia and hypochloremia (6). Stein et al. (35) performed radioisotope studies to measure blood volume in nine AIP patients. All had low blood volumes, ranging from 67% to 97% of normal, despite normal electrolytes in some patients. Although the syndrome of inappropriate secretion of antidiuretic hormone is well described in acute porphyrias, presumably due to hypothalamic involvement, hyponatremia with appropriate antidiuretic hormone levels occurs more often (34–36).

Laboratory diagnosis of porphyric crisis can involve fecal analysis (32) but most frequently involves quantification of urinary porphyrin and porphyrinogen precursors (37). These can be markedly increased during an attack, but may return to normal during remission. This normality can create a difficulty in early and accurate diagnosis in high-risk groups, such as in patients with a strong family history of porphyria. Many carriers of the trait can thus remain asymptomatic unless exposed to precipitants.

One technique known as gene linkage analysis offers a new approach to the diagnosis of acute intermittent porphyria and relies on direct complementary deoxyribonucleic acid sequencing (20,22). It does not depend on urinalysis, but rather on polymorphic markers within the porphobilingen deaminase gene (21). This permits unequivocal and early detection of carriers. Early and accurate detection of the disease in high-risk patients is of obvious benefit to safer anesthetic management of those affected and constitutes a major breakthrough in terms of perioperative anesthetic management.

Preoperative Evaluation

Acute Abdomen and Porphyria

The following symptoms should raise suspicion of porphyria in patients with acute abdominal pain: mental status changes (confusion, hysteria), peripheral neuropathy (motor > sensory), dark-colored (red to purple) urine, and known family history of porphyria (38). Of special concern is the parturient with acute abdominal pain. Greater than 50% of pregnant women who have porphyria will experience a crisis during pregnancy. If the patient with an acute abdomen, pregnant or not, does not have suggestive symptoms of porphyria, anesthetic drugs and therapies should not be modified (40).

Known Acute Porphyria

In the setting of known acute porphyria, perhaps the most difficult situation is when an acute attack is caused by and is concurrent with a disease process which mandates surgical intervention; i.e., the infection, pyrexia, and anorexia of acute appendicitis inducing ALA synthetase and precipitating crisis.

Neurologic evaluation should focus on mental status and peripheral neuropathy. If an acute crisis is suspected, attention to cranial dysfunction and bulbar symptomatology may predict impending respiratory failure.

Premedication is important, as pyschologic stress alone has been reported to precipitate crises (18,34,36). Many reports have implicated benzodiazepines (4,41,42), and their use is discussed below. Narcotics are safe in porphyria, with the exception of pentazocine, a partial agonist. Scoplamine and atropine are considered safe. Acceptable nonnarcotic sedatives include droperidol, promethazine, chloral hydrate, and diphenhydramine.

Intraoperative Management

Regional Anesthesia

Acute porphyria is not an absolute contraindication to regional anesthesia but in the setting of peripheral neuropathy, detailed preoperative exmination and documentation is essential. Potential mental status changes and patient cooperation is especially important in this setting. Bupivacaine is considered safe for regional anesthesia. Although some evidence suggests that lidocaine may increase ALA synthetase activity in animal tissue culture cells, no clincial exacerbations have been reported after the administration of ester or amide local anesthetics (1,43). Procaine decreases ALA synthase activity in the rat liver experimental model (43).

Regional anesthesia should probably be avoided in the setting of acute porphyric crisis. Associated neuropathy may be rapid in onset, clouding the differentiation between regional anesthetic onset and progressive porphyric neuropathy. In addition, mental status changes often make porphyric patients uncooperative. Finally, hypovolemia and a labile autonomic response, characteristic of acute porphyric crisis, increase the risk of hemodynamic instability in the setting of a sympathectomy. In fact, there are no studies specific to this issue—probably secondary to the ethical and medicolegal issues surrounding the institution of regional anesthesia while acute neurologic deterioration is occurring.

Induction of Anesthesia

Thiopental has accounted for the majority of drug-precipitated attacks (15,35) but the multifactorial nature of porphyric crisis makes interpretation of isolated cases difficult (18). Since dehydration, infection, fever, and endogonous steroid hormones themselves induce ALA synthetase, virtually any drug administered to a patient entering a porphyric crisis implicates that drug as a "trigger" (18).

Interestingly, even a known trigger may not induce an attack (5,44). For example, Ward (40) reviewed 36 cases of barbiturate induction of general anesthesia in patients with porphyria. None had a postoperative porphyric crisis. In another study, thiopental was administered to 27 patients with an acute porphyria but not in crisis (5). None of these patients developed an attack postoperatively. Of 10 patients who were in acute crisis prior to anesthetic induction with thiopental, however, seven had worsening of porphyric symptoms (5). These results suggest that administration of porphyrinogenic drugs does not, by itself, determine whether an attack will occur. Administration of such drugs is therefore probably only one factor that may precipitate crisis. Therefore, although thiopental will not alway precipitate crisis, barbiturates are contraindicated in known porphyric patients (9).

Benzodiazepines vary in their porphyrinogenic potential. Diazepam has been implicated as a "trigger", as have chlordiazepoxide, flunitrazepam, and nitrazepam (1,6). However, diazepam has been safely used during porphyric crises (41). Midazolam has been used safely for induction of anesthesia in patients with confirmed VP, as has lorazepam (45).

Etomidate is porphyrinogenic in animal models (46). One case has been reported of its use for induction in a latent porphyria patient with an uneventful clincial course, but at least one human porphyric crises has been reported after its use (47).

Ketamine has been implicated as triggering porphyric crisis (18). Laboratory investigation of tissue

culture results are controversial, as ketamine appears to be porphyrinogenic at higher concentrations, but not at clinical levels (46,48–50). The validity of extrapolating such *in vivo* or *in vitro* animal studies to the clinical human setting is questionable. Many consider ketamine to be safe in porphyrias (18,51,52).

Propofol has been suggested as an alternative drug to induce anesthesia. Many porphyric patients have received propofol with no clinical evidence of resultant acute crisis (46, 53–62); ALA synthetase is not induced in animal models (63,64). A prospective clinical trial of 13 VP patients showed no evidence of porphyrinogenicity when propofol was used for the induction of anesthesia (7). A single recent case report of a patient with VP noted modest increases of urinary porphyrins after a propofol infusion (33). However, as was pointed out by Harrison et al. (1) and Meissner et al (7) this increase occurred after the third consecutive anesthetic and was not accompanied by any symptoms Propofol is therefore considered "probably safe" although careful monitoring for porphyrinogenesis after anesthesia is suggested (1).

Maintenance of Anesthesia

Volatile anesthetics are generally considered safe in porphyric patients. Reports of a possible association of halothane with crises contradict both experimental and clinical experience (3,18). Neither isoflurane nor enflurane exacerbate porphyric crisis in humans (3,18). However, enflurane has been classified as porphyrinogenic based on animal data (43,65). Nitrous oxide and opioids are considered safe (9).

d-Tubocurarine and succinylcholine have been used extensively and are safe (9). Whether there is any degree of hyperkalemic response to succinylcholine is not known, but, again, succinylcholine has been used extensively and is considered safe in porphyrics. Other muscle relaxants reported as safe include vecuronium and atracurium (1,66). It is interesting to note that some steroids are considered unsafe in porphyria. Vecuronium and pancuronium share a steroid structure, but only the latter has been incriminated as unsafe based on data obtained from animals (1,25,41). Long-term experience and definitive data are lacking.

Treatment of Complications

Hypertension and tachycardia are common features of an acute attack and β-adrenergic blockers are the most appropriate therapy (38,67–69). Propranolol decreases ALA synthetase activity and increases intracellular heme levels in tissue culture (19). It is not known definitely whether these effects occur with other β-adrenergic blockers, such as labetalol or esmolol, but atenolol, a selective β_1-adrenoceptor blocker, is safe (6). α-Methyldopa is contraindicated—with both clinical and laboratory reports implicating it in porphyric crisis (9). Hydralazine is also associated with laboratory evidence of porphyinogenicity (9).

Since 20% of patients in porphyric crisis develop generalized convulsions, safe anticonvulsant therapy is necessary. Standard anticonvulsants including dilantin, barbiturates, and diazepam are safe (41,70). Bromides are effective oral treatment for chronic management but are not available for acute seizure management. Diazepam has been recommended for acute seizures despite reports of porphyria crises after its administration (3,4,41,71). Magnesium sulfate is effective in hypomagnesemic porphyria patients (72).

Monitoring

Hypovolemia and autonomic neuropathy with labile hypertension suggests the value of invasive blood pressure monitoring during an acute crisis. Central venous pressure monitoring may be warranted in the setting of ischemic cardiac disease, clinical findings consistent with heart failure, and procedures where excessive blood loss or fluid shifts are anticipated. There is no documentation of a primary cardiomyopahty associated with this disease. The cardiovascular manifestations seen are secondary to its autonomic nervous system manifestations aggravated by electrolyte disturbances described above. These may have greater implications in the presence of co-existing cardiac disease.

Postoperative Management

Monitoring for the potential onset of porphyric crisis should be continued for up to 5 days, since onset may be delayed. The onset of crisis may be heralded by either neurologic signs or autonomic nervous system stimulation (16). In such patients, appropriate cardiovascular monitoring may include electrocardiography, as well as a pulmonary artery catheter, to evaluate cardiac function and aid in the diagnosis and treatment of cardiac failure.

Cardiovascular monitoring in the setting of an acute attack should be continued postoperatively—the extent determined by clinical circumstances. The incidence of postoperative cardiac failure after acute porphyric attack is unknown. The institution of invasive monitoring of volume status should be guided by the type, duration, and extent of surgery and blood loss and the clinical status of the patient postoperatively. Neurologic status should be assessed frequently postoperatively. If antiemetic therapy is indicated, metoclopramide probably should be avoided, but promethazine, droperidol, or chlorpramazine are acceptable (see below) (6).

Treatment: Acute Crisis

Management of acute porphyric crisis involves specific attempts to reverse factors which increase ALA synthetase activity, withdrawal of offending drugs, treatment of symptoms with appropriate medications, and appropriate patient monitoring. Primary treatment directed at reversing the disease process includes hydration, electrolyte monitoring, administration of glucose (20 g/h), propranolol (which may decrease enzyme activity as well as control tachycardia), treatment of underlying infection and heme—which directly increases negative feedback to ALA synthetase (4–6).

Hematin, the preparation used most often in the treatment of porphyria, is standard therapy, but probably not the best. Hematin has produced dramatic clinical improvement, with marked decreases in urinary aminolevulinic acid and prophobilinogen excretion (67). Associated problems with hematin, however, are significant and include renal failure, thrombophlebitis, and dose-related coagulopathy (11,73,74). These negative side effects are largely secondary to the inherent instability of the compound in the infusate. The shelf-life of hematin is only approximately 3 mo.

These problems and this instability has led to the introduction of another heme compound, heme arginate. Heme arginate is more stable in solution, has a shelf-life of approximately 2 yr, and does not share the undesirable side effects profile of hematin (75).

The response to heme therapy usually occurs within 2–4 days after the start of infusion. Hematin suppresses endogenous heme synthesis and decreases significantly the excretion of ALA and PBG. The only commercial preparation in the United States is Panhematin® (Abbott Laboratories, Chicago, IL) at a dose 3–4 $mg \cdot kg^{-1} \cdot day^{-1}$ (73). Parenthetically, it is interesting to note that this was the first drug approved through the Orphan Drug Act.

Up to 48 h of initial treatment without hematin has been recommended by some, withholding its use for refractory or rapidly progressing cases (76). Recent information however, suggests that the early administration of heme arginate shortens hospitalization and improves outcome (75). At this time, however, heme arginate, the most stable form of the compound, lacks approval by the Food and Drug Administration and is not available except for research purposes in the United States. Clinical trials are scheduled to begin at the University of Texas Medical Branch at Galveston in the future.

Cimetidine may have a role in the treatment of acute intermittent porphyria by inhibiting heme oxidase activity, decreasing heme consumption and inhibiting ALA synthetase through a negative feedback mechanism (77). This apparent efficacy led to the supposition that cimetidine may be useful as a prophylactic drug, stabilizing and prolonging periods of remission. Initial laboratory and animal experiments were positive, but human studies have not been confirmatory. Although cimetidine does not worsen the clinical course and can be safely used as an H2 antagonist in patients with AIP, it does not appear to be effective prophylactic therapy (78).

Pain associated with an acute attack may require opioid therapy. Nausea and vomiting should be treated with promazine, chlorpromazine, or prochloroperazine, rather than metaclopramide, which is porphyrinogenic (6). Should bulbar symptoms appear, frequent scrutiny for respiratory failure should be undertaken. Arterial blood gas analysis and serial forced vital capacity measurements are often important adjuncts. In patients with a history of coronary artery disease, tachycardia and hypertension characteristic of the acute crisis increase myocardial oxygen demand and should be avoided.

Mortality in porphyic crises is about 10% with current treatment regimens and is primarily due to two factors: underlying infectious processes and respiratory failure secondary to depression of central respiratory drive or respiratory muscle paralysis (4). Cardiac arrest has been reported in severely affected patients with flaccid quadriplegia, coma, and bulbar symptoms (18). The presence of severe dysrhythmias may preced refractory cardiac arrest (12,35).

Further Investigation

Large clinical studies on the use of ketamine, propofol, etomidate, and volatile anesthetics are needed. Only anecdotal clinical reports attest to the safety of these anesthetics. Neither laboratory nor clinical investigation of the use of atracurium or vecuronium in porphyria is available. The lack of significant hemodynamic alterations with these drugs makes their availability particularly desirable in this group of patients.

Summary

Four hereditary types of porphyria are now classified as acute porphyrias. Enzymatic defects result in accumulation of porphyrin precursors (usually ALA and PGB). The quantity of these precursors may be normal or slightly increased in latent periods but increase to toxic levels during a porphyric crisis. Iatrogenic induction of ALA synthetase by administration of certain triggers (classically barbiturates) is only one of several factors which contribute to porphyric crisis. Signs and symptoms of acute porphyric attack consist primarily

of neurologic dysfunction, which occurs secondary to neurotoxicity of ALA or diminished intraneuronal heme levels.

Appropriate anesthetic management of porphyria requires knowledge of the type of porphyria (acute vs non-acute), assessment of latent versus active (crisis) phase, awareness of clinical features of porphyric attack, and knowledge of safe pharmacologic intervention.

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