:: Acute hepatic porphyria neuro-visceral crisis

- This document is a translation of the French recommendations drafted by Prof. Jean-Charles Deybach and Dr. Hervé Puy, reviewed and published by Orphanet in 2007.
- Some of the procedures mentioned, particularly drug treatments, may not be validated in the country where you practice.

- See also the emergency guidelines for cutaneous porphyrias

Synonyms:
Acute intermittent porphyria, Hereditary coproporphyria, Porphyria variegata

Definition:
Porphyrias are monogenic and autosomal genetic conditions and each is linked to a deficiency of haem metabolising enzymes.
Acute porphyria with abdominal pain and/or neuro-psychiatric symptoms can cause serious emergencies and include:
- Acute intermittent porphyria (AIP),
- Hereditary coproporphyria (HC),
- Porphyria variegata (PV).
Porphyria variegata and Hereditary coproporphyria can have mixed cutaneous and/or neuro-psychiatric symptoms.

Further information:
See the Orphanet abstract

Pre-hospital emergency care recommendations
Call for a patient suffering from
acute hepatic porphyria neuro-visceral crisis

Synonyms

- Acute intermittent porphyria, hereditary coproporphyria, porphyria variegata

Aetiology

- Deficiency of an enzyme involved in haem synthesis

Special risks in an emergency

- painful abdominal syndrome, psychiatric problems, motor system problems
- occasionally: port-coloured urine, tachycardia, arterial hypertension, excess sweating

Frequently used long term treatments

- no curative treatment

Complications

- contra-indicated drugs: list on www.porphyria-europe.com and www.drugs-porphyria.org
- be suspicious of neurological signs even if minor (gravity) and water and electrolyte imbalance
- be careful: depending on the sources (official websites) the list of authorised, uncertain or contra-indicated medicaments are not identical

Specific medical care prior to hospitalisation

- no vital risk other than haematological and hepatic risks
- contra-indication: barbiturates, etomidate, ketamine, sulfamides, photosensitisers…
- authorised drugs: morphine, fentanyl, midazolam, succinylcholine, vecuronium, atracurium…
- no specific treatment prior to hospitalisation
- orientation: emergency department, resuscitation if neurological signs

For further information

- www.orpha.net
- www.porphyria-europe.com
- www.porphyrie.net
- www.drugs-porphyria.org

Recommendations for hospital emergency departments

Emergency situations

1. Painful abdomen syndrome

Consider an acute hepatic porphyria crisis when faced with an unexplained severe abdominal pain: intense **pain**, developing continuously or paroxystically, diffuse (without predominant location), sometimes associated with lumbar pain radiating down lower limbs, **nausea then vomiting** which may result in major water and electrolyte disorder and chronic **constipation** sometimes alternating with bouts of diarrhoea.
In 80% of cases, it affects a young woman between 15 and 45 years old and during the menstrual period. Occasionally, **myalgia, tachycardia, arterial hypertension, excess sweating**, often without fever, can be observed and are caused by involvement of the sympathetic nervous system.

2. Psychiatric syndrome

It is very variable: it may be limited to mood problems (irritability, emotional or depressive features and, especially, major anxiety). **More rarely, there are acute psychiatric symptoms** (auditory or visual hallucinations, disorientation, confused state, delirious flushes).

3. Neurological syndrome

Neurological involvement rarely is the presenting feature and this is usually triggered or aggravated by inappropriate therapies administered without knowing the diagnosis. The neurological syndrome is very variable and can involve peripheral and/or central nervous systems: **paralysis** which is the dominant sign (discrete paresis of a small group of muscles such as the central digital extensors in the hand similar to chronic lead poisoning) or flaccid ascending paralysis of the limbs with intense subjective sensation problems and amyotrophy); **myalgias, paresis, convulsive crises** frequently associated with a **hyponatraemia** evoking a SIADH and often treated by barbiturates (main porphyrinogenic molecules).

Any involvement of the nervous system requires hospitalisation in the critical care unit as these conditions may be fatal (bulbar involvement, respiratory paralysis) or be associated with the risk of severe motor system sequelae.

- **Emergency diagnostic measures**
  - **Confirm the diagnosis:**
    - Look for an increased level of precursors in the **urine**: aminolevulinic delta acid **ALA** and porphobilinogene **PBG** (the porphyrin concentration in urine is of no use at this stage). **If the precursors are normal, it is not an acute porphyria crisis** and another cause must be looked for. **If the precursor levels are elevated, then the diagnosis of acute porphyria crisis is confirmed.** If this analysis is not available at the hospital, send a urine sample by post to a specialised centre. **A diagnosis of acute porphyria crisis requires the urgent hospitalisation of the patient.**
  - **Evaluate the severity:**
    - Intensity of painful abdomen syndrome
    - Neurological complications (check initially then re-evaluate twice a day)
    - Water and electrolyte complications (electrolytogram looking for a type SIADH hyponatraemia)
  - **Emergency investigations:**
    - Eliminate triggers: alcohol, oestrogens, porphyrinogenic drugs (Lists on www.porphyria-europe.com and www.drugs-porphyria.org), low calorie diet, undernutrition, inflammatory syndrome, concurrent infection, emotional shocks, family history suggesting porphyria crises…)

Immediate therapeutic measures

An acute porphyria crisis is a metabolic medical emergency that should be treated in hospital in a medical critical care unit. As soon as the diagnosis is considered and before receiving the results of urinary ALA and PBG, symptomatic treatment should be started in the emergency department to avoid neurological complications developing.

- **Symptomatic treatment:**
  - Search for and **eliminate the triggers**
  - **Manage the pain**: Opiate analgesia (Morphine: 1 sub-cutaneous injection every 4 hours until the pain subsides).
  - **Manage the anxiety**: Sedative neuroleptic chlorpromazine: 50-100 mg/24h or cyamemazine: 100/200 mg/24h)
  - **In the event of vomiting**: 5HT3 receptor antagonist such as ondansetron: 1 ampoule 8mg by slow IV
  - **Provide a large carbohydrate supply**: 300 - 400 g glucose per 24 hours by perfusion with monitoring by blood electrolytograms (attention to NaCl and K supply)
- Aetiopathogenic treatment:
  - R**eserved for acute porphyria crises that have been biochemically confirmed** by a significant increase in urinary precursors (ALA x10 and PBG x50 compared to normal levels). It can be started in the emergency department or the admissions service.
  - Administer **haem-arginate** 3-4 mg/kg/day for 4 days by intravenous perfusions with the aim of restoring the intracellular haem reserves. This treatment results in a spectacular improvement within 48 - 72 hours that is both clinical and biochemical. The effectiveness of haem-arginate is even greater the earlier it is used and when the average hospital stay is 4 days; on the other hand, its effectiveness is much less certain when neurological complications are involved and the hospital stay is much longer.
  - **Contact a specialised centre.**

Drug interactions

- The acute porphyric crisis is often triggered by alcohol or use of drugs that require hepatic induction of some P450 cytochromes (barbiturates, sulfamides, oestro-progestatives…).
- The **list of authorised, uncertain and contra-indicated drugs is available on** www.porphyria-europe.com and www.drugs-porphyria.org

Anaesthesia

When a porphyric patient is going to be given an anaesthetic, it is recommended that a specialised centre is contacted.

- **Cutaneous hepatic vesicular porphyria (cutaneous porphyria, hereditary coproporphyria, porphyria variegata)**
  - **Epidural / spinal nerve block: Bupivacain** is authorised
  - **General anaesthesia:** the anaesthetist should **contact a specialised centre in all cases**
  - **Cutaneous surface anaesthesia: Bupivacain and local anaesthetic cream** are authorised.
  - **Dental anaesthesia: Articain + epinephrine** is authorised on **healthy carriers or** patients in **long remission.** A urine sample should be taken from the first micturition the following day and sent to a relevant centre. However, all chronic cases (recurring acute crises) should be discussed with a doctor of a specialised centre.$

Additional therapeutic measures and hospitalisation

- The family must be advised and made aware of the situation during screening and given the contact details for a reference centre that the family should consult at least once.

Organ donation

- Despite there being little published data, as it is a hepatic metabolic condition sometimes associated with a moderate renal insufficiency, **common sense suggests that it is not wise to offer a liver or kidney from a porphyric patient** to a recipient.

Documentary resources

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