British Inherited Metabolic Disease Group

ACUTE PORPHYRIA
ADULT EMERGENCY MANAGEMENT

IMMEDIATE ACTIONS

For patients in England, Scotland and Wales, please contact the National Acute Porphyria Service (NAPS) for advice:

Within working hours: phone the NAPS team responsible for treating the patient.
King's College Hospital, London – 02032 995 776 or University Hospital of Wales, Cardiff – 02921 846 588

Out of working hours (or new patients at any time): An emergency service is provided 24 hours a day, 7 days a week. The University Hospital of Wales switchboard (02920 747 747) will provide contact details for the on call NAPS team.

BACKGROUND:

The acute porphyrias (acute intermittent porphyria, variegate porphyria, hereditary coproporphyria) are autosomal dominant conditions. Patients are at risk of acute neurovisceral attacks, which may be life threatening. Acute attacks are uncommon and do not affect all those who inherit the condition. It may be difficult to distinguish between an acute attack and other causes of acute abdominal pain. Acute attacks may be precipitated by infection, stress, unsafe prescribed or illicit drugs, dieting or excess alcohol consumption. Multiple factors may be involved, or there may be no obvious precipitating event. The symptoms and signs are due to neuronal dysfunction affecting the autonomic, and/or motor and/or central nervous system.

Detailed information on diagnosis and treatment of acute porphyria is available at:
www.porphyria.eu/

The current list of drugs considered safe to use in acute porphyria can be found at:
https://www.wmic.wales.nhs.uk/specialist-services/drugs-in-porphyria/

CLINICAL FEATURES:

An acute attack of porphyria almost invariably starts with constant abdominal pain, which becomes progressively more severe and is associated with nausea, vomiting and constipation. The patient may also complain of pain in the lower back, buttocks and thighs. The abdominal pain is diffuse with no localising signs or evidence of an acute abdomen on examination. The level of pain appears out of keeping with the physical signs and requires large doses of parenteral opiate administration for effective relief. This may require support from the pain team.
Other symptoms and signs include:

- hypertension and tachycardia
- seizures (which may be related to hyponatraemia)
- muscle weakness (which may progress to flaccid paralysis and respiratory insufficiency)
- psychiatric symptoms such as agitation, insomnia, confusion, psychosis

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RECOMMENDED MANAGEMENT

CLINICAL ASSESSMENT

- Assess general condition and analgesic requirement
- Monitor pulse and blood pressure
- Check motor power and ventilatory function
- Review all prescribed medication
- Consider and remove possible precipitating factors (unsafe drugs, alcohol, fasting, infection)
- Consider and exclude other causes of abdominal pain

INITIAL INVESTIGATIONS

- **Blood Tests:**
  - Full blood count
  - Urea & electrolytes

Severe hyponatraemia can evolve rapidly, leading to seizures. During the acute phase of illness we recommend monitoring sodium at least every 12-24 hours

- **Urine Tests:**
  - Urine porphobilinogen (PBG)

Collect a 10ml random urine sample in a plain labelled tube and protect from light prior to analysis. The sample should be collected before starting haem arginate. In known porphyria patients, treatment should not be delayed while waiting for the result.

- **Other tests as indicated by clinical findings** (e.g. CRP, infection screen)

TREATMENT

- **Analgesia**

Opiates are almost always indicated and should be administered regularly. Subcutaneous or oral routes are preferred when possible.
Consider a morphine PCA if pain is severe.
Dihydrocodeine and morphine are safe. Pethidine should be avoided.

- **Maintain fluid and calorie intake**

If tolerating oral intake – encourage carbohydrates
If not tolerating oral intake – start intravenous 0.9% sodium chloride containing 5% glucose or 0.9% sodium chloride alone (maintenance 2 litres per day). Avoid intravenous glucose in water solution, including dextrose 5% and 10% as this can precipitate/exacerbate hyponatraemia.

- **Treat symptoms as indicated**

Using medications that are safe in porphyria such as:
Vomiting - ondansetron, cyclizine, prochloperazine
Agitation - chlorpromazine
Seizures - diazepam, clonazepam, magnesium sulphate
Hypertension/tachycardia - propranolol, labetalol
Constipation - bulk laxatives, senna

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- **Consider treatment with Haem arginate (Normosang®)**

Haem arginate is indicated if any of the following symptoms are present: severe persistent pain, persistent vomiting, neuropathy, seizures, hyponatraemia, psychosis, severe hypertension and tachycardia.

Administration:

- Intravenous haem arginate (Normosang, Orphan Europe, UK) is available as stock solution at 25mg/ml. This is supplied free of charge through the NAPS service for all patients living in England, Wales and Scotland. The service does not cover patients in Northern Ireland.
- Dose: 3 mg/kg daily (up to maximum of 1 vial/250 mg daily) on 4 consecutive days
- Dilute immediately before use in 100ml 0.9% sodium chloride solution and protect from light
- Infuse intravenously over 30-60 min via a large vein using a giving set with a 15-20 micron inline filter
- **Promptly** flush the line with 250ml 0.9% sodium chloride solution (initially 3-4 boluses of 10ml, then remainder under gravity)
- Side effects are unusual apart from thrombophlebitis at the site of administration (see below)

Haem arginate carries a risk of significant extravasation injury with thrombophlebitis at the site of administration being a common issue.

Complications may be limited by the following measures:

- Administer the infusion through a PICC/CVC line. This is the preferred route
- If administering the infusion peripherally, a large venflon should be used in a large vein and consideration given to cannula site (e.g forearm rather than hand or deep ACF vein)
- Vascular complications may be reduced by alternating arms for consecutive infusions, and diluting haem arginate in 20% albumin
- The infusion site should be observed regularly throughout the infusion. If the patient reports pain at the infusion site, or there is noticeable oedema or redness, **stop the infusion immediately** and follow local extravasation guidelines