Gabapentin Reduces Neurovisceral Pain of Porphyria

Yu-Chien Tsao¹³, Dau-Min Niu²³, Jen-Tse Chen¹³⁴, Chia-Yi Lin¹³, Yung-Yang Lin¹³, Kwong-Kum Liao¹³

Abstract-

Purpose: Gabapentin is well known for pain control. Here, we report that gabapentin is a good adjunct for visceral pain in a porphyria patient.

Case report: A young female was admitted due to acute abdomen. On admission, she was noted to have hyponatremia, tachycardia, and hypertension. Then, she had episodes of seizure and confusion. Gabapentin was prescribed for the control of seizure and pain before the diagnosis of acute intermittent porphyria was confirmed. Seizure did not occur after gabapentin. Pain severity also significantly reduced with visual analogue scale from 10 to 4. The severity of pain rebounded after gabapentin was withdrawn. When the diagnosis was proved, the neurovisceral pain further decreased with combination of morphine and gabapentin and subsided after treatment with hematin.

Conclusion: Our report indicates that gabapentin can be considered in porphyria patients, especially when patients had seizures or acute abdomen, when morphine is not available or contraindicated, when abdomen pain transforms as chronic pattern, and when neuropathic pain occurs in extremities.

Key Words: acute abdomen, acute intermittent porphyria, gabapentin, pain, seizure

Acta Neurol Taiwan 2010;19:112-115

INTRODUCTION

Acute intermittent porphyria (AIP) is a rare autosomal dominant metabolic disorder affecting the production of heme, the oxygen-binding prosthetic group of hemoglobin¹. It is characterized by a deficiency of the enzyme porphobilinogen deaminase. Under normal circumstances, heme synthesis begins in the mitochondrion, proceeds into the cytoplasm, and finishes back in the mitochondrion. However, without porphobilinogen deaminase, a necessary cytoplasmic enzyme, heme synthesis cannot finish, and the metabolite porphobilinogen accumulates in the cytoplasm⁰. Additional factors must also be present such as hormones, drugs, and dietary changes that trigger the appearance of symptoms.

The most common initial symptom of AIP is abdominal pain, which is present in 90% of patients. Other common gastrointestinal symptoms include nausea/vomiting (43%), extremity pain/parasthesias (50%), and constipation (48%)⁰. Here, we reported that...
gabapentin not only reduced the seizure attacks but also the abdomen pain of an AIP patient.

**CASE REPORT**

A 24-year-old female was admitted because of colic abdominal pain. She had amenorrhea and was noted to have lower luteinizing hormone (0.01 mIU/ml; reference 0.5-5 mIU/ml) and lower follicle-stimulating hormone (0.08 mIU/ml; reference 1.8-10.5 mIU/ml) 4 weeks before admission. Then, she had hormone therapy, i.e. utrogestan E2 100mg a day, progesterone injection 25mg per cc, and clomifene (Clomid) 100 mg a day. At follow-up visits, she reported poor appetite, cold sweats, light headedness, generalized weakness, nausea, vomiting, constipation, episodes of tachycardia, and suprapubic and epigastric pain. She did not have dysuria, headache, or double vision. Her family did not have similar history. On examination, besides ill looking, she was noted to have hypertension and tachycardia. However, she did not have rebound tenderness or guarding. Routine serum biochemistry showed significant data as follows: Na 101 mmol/l (135-145), K 2.8 mmol/l (3.4-4.7), albumin 3.6 g/dl (3.7-5.3), total protein 5.2 g/dl (6.4-8.4), BUN 3.1 mg/dl (7-20), creatinine 0.43 mg/dl (0.5-1.2), lipase 635 U/L (< 190), amylase 286 U/L (< 180), Urine osmolality was 652 mOsm/Kg H2O (random 50-1200; 24-hour 300-900), and serum osmolality was 210 mOsm/Kg H2O (275-295). Oral intake of water was restricted, and sodium chloride tablets and hypertonic saline were administered. Magnetic resonance imaging and computed tomography of the abdomen did not show any significant abnormalities. There was no evidence of bowel obstruction or intra-abdomen fluid collection.

![Graph](image1.png)

**Figure 1.** The diary of pain along with the dosing of gabapentin through the hospital days. VAS: visual analogue scale; DC: discontinue.
Intravenous fluids and acetaminophen were given but did not reduce her pain. She cried and bumped her head against the pillow on the bed when the severity of pain was up to 10 of visual analogue scale. She described that she never experienced such kind of pain before.

She had episodes of seizure after admission. The first attack was on the 4th hospital day. She fell while walking and had generalized tonic seizures and lapsed into confusion for a few minutes. Electroencephalographic findings were normal. Neurological examination on the 5th hospital day showed that the cranial nerves were normal; motor strength was 4+ out of 5 in the arms and in the legs. Deep tendon reflexes were normal in both legs. Sensation was normal with respect to temperature, vibration, proprioception, and light touch, but sensation to pinprick was decreased in the trunk and pelvic girdle. The impression of acute intermittent porphyria was made. Before the diagnosis of porphyria was confirmed, gabapentin (Neurontin, Pfizer, USA) was prescribed for the control of seizure and the pain. Seizure did not occur after gabapentin and pain severity also significantly reduced (Figure 1). Because of no more seizure, the patient and her parents decided to discontinue gabapentin on the 14th hospital day and prepared for discharge. Unfortunately, the acute abdomen rebounded within 12 hours of withdrawal (Figure 1). Gabapentin was reinstituted later.

On the 17th hospital day, the diagnosis of porphyria was confirmed by decreased serum porphobilinogen deaminase activity of 25.9 nmol/hr/ml RBC (normal, 30.3-73.7 nmol/hr/ml RBC) and positive urinary porphyrinogen. Her urine turned red when exposed to light and the Watson-Schwartz test was positive. After the diagnosis was made, hemin (4 mg/kg/day) and morphine were immediately begun. The neurovisceral pain further decreased with morphine and subsided after treatment with hemin.

**DISCUSSION**

**Pain mechanism of acute abdomen of porphyria**

The pain mechanism is not yet clear in acute porphyria. Autonomic dysfunction was inferred as the main cause of acute abdomen, tachycardia, urinary retention, incontinence, hypertension, and postural hypotension. The pathological related findings are chromatolysis of sympathetic ganglion cell and celiac ganglion. A further support is from a clinical observation that the treatment of neurovisceral pain of AIP was successfully achieved with celiac plexus neurolysis. AIP patients that experience frequent attacks can develop chronic pain in the gut, as well as chronic neuropathic pain of limbs. This is thought to be due to small fiber neuropathy.

**Gabapentin for neurovisceral pain**

Gabapentin has been studied in visceral hypersensitivity, such as interstitial cystitis, overactive bladder, and irritable colon syndrome. These three conditions share a similar pathophysiology of up-regulation of afferent C-fiber sensory neurons. In the study of overactive bladder, 14 of 31 patients had significant improvement with gabapentin. In the study of interstitial cystitis, pain reduced in 10 of 21 patients. Although the mechanism of gabapentin for pain control has not been fully elucidated, it appears to be the inhibitory activity on afferent C-fibers activity.

*Gabapentin in combination with morphine*

Our report indicates that gabapentin is an option in providing relief for pain caused by porphyria. Morphine
is a safe analgesic and is widely applied in the pain control of acute prophyria\(^{18}\). Gabapentin combined with morphine achieved better analgesia at lower doses of each drug than each drug alone, with only mild adverse effects\(^{19}\). Hence, gabapentin is sincerely suggested for AIP patients, especially when patients had seizures and acute abdomen, when morphine is not available or contraindicated, when abdomen pain transforms as chronic pattern, and when neuropathic pain occurs in extremities.

**REFERENCES**