Risk of phenibut use in a patient prescribed gabapentinoids
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Background
- Increasing regulation of opioid prescriptions for pain
  → alternatives such as gabapentin and pregabalin
- Patients may seek other alternatives such as phenibut, a drug marketed as a nootropic supplement
- We present such a case in a patient with chronic pain

So, what is phenibut?
Phenibut (β-phenyl-y-aminobutyric acid or β-phenyl-GABA) is a synthetic GABA-mimetic developed in Russia in the 1960s. Phenibut acts as a central nervous system depressant, like baclofen or gabapentinoids, primarily at GABA-B though also at several other receptors.

It is marketed for nootropic (neurocognitive enhancement), anxiolytic, and sedative effects, and trends show increasing use in the past few years. Because the United States (US) Food and Drug Administration (FDA) views phenibut as an amino acid, the substance is not regulated. Online retailers sell it as a dietary supplement in the US and elsewhere despite known risk of dependence, overdose, and withdrawal.

Case report
- **Patient:** 30-year-old veteran with chronic neuropathic pain related to an MVA
  - **Prior meds:** analgesics including gabapentin and pregabalin, which he at times misused to seek pleasurable intoxication
  - **Phenibut exposure:** after he developed tolerance to pregabalin, he purchased phenibut powder online seeking analgesia and anxiolysis

  **Effects noted by our patient when using phenibut**

<table>
<thead>
<tr>
<th>Beneficial</th>
<th>Bothersome*</th>
<th>Withdrawal</th>
</tr>
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<tbody>
<tr>
<td>relief of chronic nerve pain</td>
<td>↑ emotionality (particularly irritability)</td>
<td>- hot flashes</td>
</tr>
<tr>
<td>anxiolysis</td>
<td>↑ libido</td>
<td>- formation</td>
</tr>
<tr>
<td>↑ tolerance when co-ingest with pregabalin</td>
<td>↑ sensation of intoxication</td>
<td>- restlessness</td>
</tr>
<tr>
<td>↓ tolerance withdrawal</td>
<td>↑ brief blackout periods</td>
<td>- nausea</td>
</tr>
<tr>
<td>- most prominent at high doses</td>
<td>- insomnia</td>
<td>- cravings to use</td>
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</tbody>
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- **Withdrawal symptoms:** appeared about 24 hours after last use. He presented to an outside hospital with suicidal ideation and seeking supervised withdrawal.
  - **Outside hospital course:** After admission he developed tachycardia, hypertension, diaphoresis, visual hallucinations, and paranoid delusions. He was placed on an alcohol withdrawal protocol with lorazepam administration for symptoms.
  - **Course at our Veterans Affairs inpatient psychiatry unit:** After transfer, he completed a taper off both lorazepam and pregabalin at his request. He was discharged to the intensive outpatient program for substance use disorders.

What is the concern with gabapentinoids?
- High comorbidity of substance use disorders occurs in patients with chronic pain.
- Gabapentinoids are also known to be misused, and a history of substance use disorder places patients at high risk for misuse of gabapentinoids.
- One United Kingdom internet study of 1,500 people reported gabapentin misuse in the general population at 1.1%.
  - With the national initiatives to de-prescribe opioid medications and increasing regulation of gabapentin in some states, many patients are perceiving barriers in access to medications they had previously used to address chronic pain.
  - The FDA recently released warnings that gabapentinoids can cause respiratory depression when used alone or with opioids.

Discussion
Patients may not be aware of the risks of addiction and withdrawal should they choose to purchase phenibut, as well as the risks of respiratory suppression when taken at high but still unregulated doses. Prescribers should be prepared to proactively educate and monitor for use throughout their clinical relationship. For patients who are using phenibut, prescribers should be prepared to manage withdrawal. Our patient was managed inpatient using lorazepam administered according to a symptom-triggered protocol, however other case reports have indicated use of phenobarbital taper or baclofen taper.

Key points
Patients prescribed gabapentinoids as an alternative to opioids may:
- perceive barriers to accessing medications with increasing regulation in some states
- seek relief with supplements not regulated by the FDA such as phenibut

Physicians prescribing gabapentinoids should:
- screen for substance use
- monitor for use of phenibut
- be prepared to provide appropriate support for issues related to addiction and withdrawal

References