Gabapentin: Treating or Causing Addiction?
Objectives

1. Evaluate and understand the abuse potential of gabapentin.

2. Identify “red flags” that may exacerbate abuse potential and increase risk of adverse effects.

3. Identify signs of gabapentin withdrawal and choose appropriate therapy to minimize hospitalization stay.
Case

A 54 year old male presents to your pharmacy requesting a refill for his gabapentin prescription. After reviewing his profile, you see that the patient is 2 weeks early for his refill, lives over an hour away, and gets his medications filled at various locations.
Gabapentin

- A central, non-selective inhibitory agent with likely GABA and non-GABA activity

- Dose: 1,800-3,600 mg/day

- Side Effects:
  - Drowsiness, dizziness, ataxia, tremor

- FDA- Approved Indications:
  - Adjunct treatment of partial seizures
  - Post-herpetic neuralgia

- Off- Label Indications:
  - 90% of sales

History

- **1994**: Neurontin® approved for marketing as adjuvant therapy to treat partial seizures
- **2002**: Approved for post-herpetic neuralgia
- **2003**: One of the 50 most prescribed drugs
- **2004**: Pfizer settles $430 million lawsuit for fraudulently promoting off-label uses
- **2004**: Generic equivalent marketed by TEVA
- **2014**: 39th most prescribed drug in the United States

http://www.pharmacy-tech-test.com/top-200-drugs.html
# What’s the Difference?

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Addiction Therapy

- Cocaine Dependence
  - ↓ Withdrawal Symptoms
  - ↓ Cravings

- Cannabis Dependence
  - ↓ Withdrawal Symptoms
  - ↑ Executive Functioning

- Other substances
  - Alcohol
  - Opioids
  - Benzodiazepines

A proof-of-concept randomized controlled study of gabapentin: effects on cannabis use, withdrawal and executive function deficits in cannabis-dependent adults. *Neuropsychopharmacology*. 2012
Substance Use Disorder

- A problematic pattern of use of an intoxicating substance leading to at least two of the following, occurring within a 12-month period:
  - Larger amounts or over a longer period of time than what was intended
  - Persistent desire or unsuccessful efforts to cut down or control use
  - Great deal of time spent doing activities necessary to obtain the substance, use the substance, or recover from its effects
  - Cravings (strong desire or urge to use)
  - Recurrent use resulting in failure to fulfill major role obligations at work, school or home
  - Continued use despite persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of its use
  - Giving up important social, occupational or recreational activities due to use
  - Recurrent use in situations which it is physically hazardous
  - Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been causes or exacerbated by the substance
  - Tolerance
  - Withdrawal

Substance Use Withdrawal

- Cessation or reduction in use has been heavy and prolonged
- Development of symptoms shortly after cessation or reduction in use
- Symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning
- Symptoms are not attributable to another medical condition and are not better explained by another mental disorder

Gabapentin Dependence, Withdrawal, Misuse & Abuse
A Review of Case Reports
Abuse: An Overview

- Gabapentin effects vary with the user, dosage, past experience, psychiatric history and expectations.

- Street Name: “Gabbie’s” & “Johnny’s”

- Examples of varying experiences reported:
  - Euphoria
  - Improved sociability
  - “Marijuana-like” high
  - Relaxation, sense of calm
  - “Zombie-like” effects
Intranasal abuse of gabapentin among inmates with prior history of cocaine abuse

- Indication: neuropathic pain, epilepsy, anxiety, mood disorders
- Only 19/96 (20%) prescription bottles dispensed were found to be in the possession of the appropriate patient
- 5 inmates admitted to widespread abuse of capsules
- Results: By the end of 2001, gabapentin was removed from the formulary

A First Case Report

67 year old white female with mood disorders and a history of alcohol abuse leading to polyneuritis

- **Gabapentin Rx:**
  - 4800 mg | Reality 7200 mg +

- **Concurrent Rx:**
  - Amitriptyline 100 mg
  - Naproxen 550 mg

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**April 2005**
Cut off by all providers and pharmacists
Withdrawal
Hospitalized

**June 2005**
Reinitiated on Gabapentin 600-1200 mg/day

**August 2005**
Increased dose
Addition of Diazepam 10 mg

**September 2005**
Patient resumed consumption of high doses

Gabapentin Induced Delirium and Dependence

- 38 year old male physician with a history of alcohol dependence, was self-administering high doses of gabapentin
  - RX: 2400 mg | Reality: 4800 mg +
  - 2 month history of confusion, attention, concentration, short term memory and occupational difficulties
  - Fired from his job
  - Met DSM-IV criteria for substance intoxication delirium and psychoactive substance dependence
  - Naranjo Score: 9

Gabapentin Induced Delirium and Dependence

*Post-Withdrawal Course*

- Dose was tapered and completely discontinued over 8 days
- Reevaluated at weeks 3 and 6
  - Reported specific and intense cravings, headaches, significant cognitive problems including attention related difficulties, anxiety, depression, tingling and experiences of depersonalization and derealization
- Reevaluated at 10 weeks
  - Reported significant improvement in mood and improved executive skills
- Week 22: requested new prescription for gabapentin
- Week 31: reported mild cravings and admitted that he was “addicted”
- Week 74: moved and relapsed on gabapentin and alcohol

Delirium Tremens

- 33 year old man with history of hepatitis C, alcohol abuse, other drug dependence and history of delirium tremens associated with alcohol withdrawal
  - **Gabapentin Rx:**
    - 1800 mg | Reality 3600 mg +
  - **Concurrent Rx:**
    - Paroxetine
    - Quetiapine

Originally

Patient started doubling daily dose to reduce EtOH craving and to “calm him”
Routinely getting early refills

Then

Doctor and physicians stopped allowing early refills
3 days off gabapentin, roommate found him disoriented and brought him to the ED

In ED...

In ED became diaphoretic, agitated, tachycardic and tremulous
Initiated on lorazepam and haloperidol for 3 days with no clinical improvement

Conclusion

Patient was reinitiated on gabapentin 300 mg Q8H
Symptoms completely resolved within 2 days

Sedated & Confused

63 year old man with chronic back pain, multiple back surgeries and history of alcohol abuse (sober 10 years)

- Gabapentin Rx:
  - 1800 mg | Reality 4900 mg

- Concurrent Rx:
  - Oxycodone

Originally

Taking higher than prescribed doses

Day of Admission

Reports taking 4900 mg for 11 days

Presents to ED after several days of fatigue, sedation and confusion

During Hospital Stay

Initiated lorazepam which caused agitation and hallucination

Increased lorazepam dose and became rapidly tachycardic, febrile & diaphoretic

Conclusion

Discontinued lorazepam

Initiated gabapentin 300 mg Q6H, quickly became lucid and stable

Patient sent home fully recovered

Tayside Studies

2009
- Out of 251 patients, 5.2% had prescriptions for gabapentin
- Mean Dose: 1,343 mg
- 3 times more likely to admit to non-medical use of analgesics than patients not on gabapentin

2011
- Autopsy of 1400 patients
- 48 had gabapentin in toxicology report with 36 including morphine and/or methadone
- Indicates recent possible opioid dependence

Summary

Though there is limited data published, there seems to be trends that may correlate to a patient being at risk for dependence that can lead to abuse and addiction:

1. History of substance abuse
2. Concurrent use of psychotropic medications
3. High doses
Future Discussion

What we can do?
- Assess patients substance use history, psychiatric history and concurrent medication before prescribing
- Monitor for early refills, limit day supply

What can be done?
- Epidemiology of misuse needs further detailed assessment to cross-link police, pharmacists, providers, patients, and members of the community
- Consider scheduling
- Establish protocol for overdose and withdrawal prevention
Back to our case...

A 54 year old male presents to your pharmacy requesting a refill for his gabapentin prescription. After reviewing his profile, you see that the patient is 2 weeks early for his refill, lives over an hour away, and gets his medications filled at various locations.

Medication Profile:
- Bupropion SA 200 mg, Take 1 tablet by mouth twice daily, # 180
- Disulfiram 250 mg, Take 2 tablets by mouth daily, # 60
- Fluoxetine 20 mg, Take 1 capsule by mouth daily, # 30
- Gabapentin 400 mg, Take 3 capsules by mouth three times daily, # 810
- Lisinopril 20 mg daily, Take 1 tablet by mouth daily, # 90
- Metformin 1000 mg, Take 1 table by mouth twice daily, # 180

The technician explains to the patient that she is unable to refill the prescription for him because he just received a 90 day supply two weeks prior. The patient becomes aggravated and starts yelling at the technician, claiming he never received that prescription. You print out the dispensing log with the patients signature on file and explain to the patient that insurance will not cover this refill. The patient becomes increasingly aggressive, calling both you and the technician derogatory terms and then storms out screaming he will go to a “better pharmacy to get this filled”. He walks back into the pharmacy 3 minutes later demanding his medication stating he will pay cash.
What is a “red flag” that indicates this patient may be abusing gabapentin?

A. Taking concurrent psychotropic medications
B. History of substance abuse
C. On high doses of gabapentin
D. Great deal of time spent doing activities necessary to obtain the substance
E. All of the above
A patient presents to your ED delirious and sedated, withdrawing from gabapentin. What is the most appropriate treatment option?

A. Lorazepam
B. Haloperidol
C. Gabapentin
D. Phenobarbital
Thank you!
Questions?
Gabapentin:
Treating or Causing Addiction?