

Concomitant use of bupropion and fluoxetine leading to symptoms of mania and serotonin syndrome

A Case Study

Haining Yu MD MPH
Psychiatry PGY-3

Intro

■ Serotonin syndrome

- Well known as a potentially life threatening syndrome precipitated by use of serotonergic drugs.
- Can present in a milder form that often goes unrecognized and unreported.
- Milder presentations may be subacute and lack the hallmark symptoms of fever, muscle rigidity.

Case

20 yo female followed in outpatient mental health clinic

- Psych history:
 - OCD
 - GAD
 - Panic Disorder
 - Excoriation disorder (skin picking)
 - Unspecified depressive disorder
- Medical history
 - PCOS
 - Migraine
 - Obesity

HPI

- Weekly CBT, high dose fluoxetine (80mg)
 - Fair to good control of anxiety, OCD, excoriation and panic symptoms
- Ongoing depressive symptoms
 - hypersomnia, anhedonia, amotivation, fatigue.
- Bupropion 150mg started leading to partial response with no adverse effects
- Bupropion then increased to 300mg after 6 weeks to improve on partial response.

HPI

- 8 days after patient noted during weekly CBT session:
 - decreased need for sleep, increased irritability, excessive spending, decreased appetite, hypersexual behaviors and impulsive use of alcohol and drugs.
 - Symptoms self-resolving. Despite psychiatrist recommendation, patient opted not to change medication regime
- 3-4 days later, mania symptoms had fully resolved, patient then noted symptoms of:
 - Headache, diarrhea, mental confusion, feeling shaky, having subjective sensation of increased HR
 - Symptoms resolved after decreasing fluoxetine to 40mg

Exam

- Mental status during the interval therapy visit was notable for **increased speech output** and increased **excitability** and **anxiety** in her affect.
- At time of next visit:
 - normal vital signs
 - Appearance/behavior: well appearing, cooperative
 - speech: normal rate, rhythm, volume and prosody
 - mood: “good”
 - affect: euthymic, calm
 - TP: linear, goal oriented
 - TC: no abnormal TC, no SI, HI, AVH
 - Cognition: intact
 - I/J: intact

Additional history

- Similar symptoms of confusion, increased HR, shakiness in response to migraine medication
- Use of psilocybin in the days prior to onset of symptoms serotonin syndrome.
- Case resolution
 - Keep lower dose of fluoxetine 40mg and bupropion 300mg XL.
 - Started this patient on a mood stabilizer (Lamictal).
 - Warned to avoid use of any additional serotonergic substances.
 - Patient continues to be euthymic, her OCD and anxiety symptoms are stable

Serotonin Syndrome

Symptom Cluster	Symptomatology
Altered Mental Status	Agitation Anxiety Disorientation Restlessness Excitement
Neuromuscular Abnormalities	Tremors Clonus Hyperreflexia Muscle rigidity Bilateral Babinski signs Akisthesia
Autonomic Hyperactivity	Hypertension Tachycardia Tachypnea Hyperthermia Mydriasis Diaphoresis Dry mucous membranes Flushed skin Shivering Vomiting Diarrhea Hyperactive bowel sounds Arrhythmias

- Serotonin symptoms can present as a range from mild to severe
 - Mild forms can be
 - Sub-acute (vs with 24H)
 - No fever
 - No obvious muscle rigidity
 - Neuro exam can reveal more subtle symptoms

Drug Interactions

- Bupropion decrease metabolism of fluoxetine
 - Increased serum levels of fluoxetine
 - CYP2D6 inhibition
 - Increase toxicity/adverse effects from fluoxetine
 - This patient more vulnerable due to high dose of fluoxetine
- Psilocybin is partial agonist for various serotonin receptors

Antidepressant induced mania

- Occurs commonly (6-8%) in patients treated with antidepressants for unipolar depression
 - Risk is lower for bupropion, mirtazapine
- Rates of switching are higher in younger people
- Risk factors
 - family history of bipolar disorder
 - onset of depression before age 25
 - recurrent depressive episodes
 - atypical features of depression such as hypersomnia