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Toxicology Sessions: Wellbutrin Toxicity

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Take Home Points

- **Bupropion is increasingly prescribed for smoking cessation.**
- **Bupropion overdose with sustained release formulations may have delayed onset of toxicity and patients should be admitted.**
- **Benzodiazepines should be used to treat seizures associated with bupropion overdose.**
- **St John's wort and linezolid are weak monoamine oxidase inhibitors and both can contribute to serotonin syndrome**

CASE

A patient presented with a bupropion overdose. He was very tachycardic. Toxicology was consulted and provided recommendations.

- **Bupropion is thought of as an atypical antidepressant but is increasingly prescribed for smoking cessation.** There are two different brand names in the US; Wellbutrin and Zyban.
- **This drug can cause seizures.** For compliance reasons, these medications are both available with sustained release formulations. This can result in recurrent seizures.
- **Bupropion overdose with sustained release may have delayed onset of toxicity.** If the patient presents to the ED after bupropion overdose, they should be admitted to a monitored setting. You can't just observe them in the ED.
- **Should you give activated charcoal?** We don't like giving activated charcoal to patients who might seize.
- **There may be a role for whole bowel irrigation.**
- **Patients may decompensate rapidly and have seizures.** If they do have seizures, the treatment is with benzodiazepines. There is no role for phenytoin or other antiepileptic medications. Nordt likes propofol for sedation if they are intubated and continue to seize.
- **Although uncommon, bupropion may have QRS widening seen on EKG.** This is often worse with seizures due to a low pH. If you see QRS widening, give bicarbonate via IV push until the QRS narrows. The target pH is 7.45-7.55. You may need to adjust the ventilator settings.
- **How much bicarbonate?** Nordt gives 1-2 amps of bicarb each time. If it doesn't narrow, he gives two amps at a time until it improves. These patients almost never get hypernatremic or hypokalemic.
- **Are there any clinical findings?** They may be somnolent. Patients may seem pretty normal until they start seizing.
- **Is there a role for Intralipid (IV fat emulsion) in refractory cases?** The first case report on Intralipid use for a non-local anesthetic poisoning was a polydrug poisoning with bupropion.
  - *Sirianni, AJ et al. Use of lipid emulsion in the resuscitation of a patient with prolonged cardiovascular collapse after overdose of bupropion and lamotrigine. Ann Emerg Med. 2008 Apr;51(4):412-5. PMID: 17766009*
  - **There isn't much evidence that Intralipid works.** That being said, if you have someone who is going to die, don't let them die without giving Intralipid.

- **MAOI may also result in overdose.** Selegiline is available via transdermal patch. MAOI poisonings are interesting. They are effective antidepressants but risky.
- **What is monoamine oxidase?** This is an enzyme that breaks down biogenic amines (such as norepinephrine, serotonin and dopamine) in the presynaptic terminal. If the enzyme is inhibited, it increases the concentration of a bunch of things that make you feel better. This is similar in effect to amphetamine.
- **There are two isoforms of monoamine oxidase**; type A and type B. You can remember A for alimentary or involving the gut. This is predominately in intestines and liver. B for brain and blood (platelets). These do different things and break down different biogenic amines to a certain extent. The original MAOIs (such as tranylcypromine, phenelzine and isocarboxazide) were non-specific for A and B. Selegiline is specific for type B because it is traditionally for Parkinson's disease. This works in the basal ganglia to increase dopamine in combination with carbidopa.

CASE

A patient overdosed with dextromethorphan in combination with several selegiline patches. The clinical picture looked like serotonin syndrome.

- **With classic MAOI toxicity, patients would sometimes develop a hyperadrenergic state.** They could present with severely elevated blood pressure and dripping sweat. Conversely, patients who took a handful in a suicide attempt could have a delay for many hours. They could have short-lived hypertension followed by complete cardiovascular collapse.
  - Nordt recommends monitoring the blood pressure and if you do treat it, use something like phentolamine.
  - If the patient becomes hypotensive, you will need to use a direct acting pressor like norepinephrine or phenylephrine because they have depleted their catecholamines.
- **Serotonin syndrome can happen with any of these drugs.** In the Libby Zion case, a young woman was on a monoamine oxidase inhibitor and was treated with meperidine for a viral syndrome. She developed serotonin syndrome and died. There are multiple drug-drug interactions that can result in serotonin syndrome.
  - The older MAOIs are very unlikely to result in serotonin syndrome at therapeutic dosages. Selegiline does have some weak monoamine oxidase A activity. The serotonin syndrome seen in the overdose with dextromethorphan and selegiline may have been due to the dextromethorphan with some contribution from the selegiline. If you have someone with serotonin syndrome, treat it as such. After the dust settles, their primary care physician or psychiatrist may want to reconsider selegiline.
  - Serotonin syndrome is a diagnosis of exclusion. They may be febrile, agitated and confused. Make sure you aren't missing meningitis. The hallmark is clonus. If they don't have clonus, they don't have serotonin syndrome.
  - If they seize, the treatment is benzodiazepines.
  - For agitation, give benzodiazepines.
  - If hyperthermic, aggressively and actively cool them. This may involve paralysis and placing them on the ventilator.
  - Cyproheptadine is a serotonin antagonist but it can only be taken orally. It could be crushed and given via a NG-tube. It is fine to give it but the natural progression of serotonin syndrome is resolution in about 12-24 hours and the cyproheptadine takes about that long to work. It is hard to say if the cyproheptadine made a difference or it was just the natural disease progression. The dose is usually 8-12 mg and can be repeated.
- **St. John's wort.** There is some evidence that it works but it is controversial if it works better than traditional antidepressants. In some of the studies comparing it to SSRIs, it has been shown as effective. Why? There are two components that we think are the active ingredients; hypericin and hyperforin. These are weak monoamine oxidase inhibitors and have both Type A and B inhibition. There are rare cases of serotonin syndrome with St. John's wort. When you perform medication reconciliation, you should always ask about herbal medications. If someone is taking St. John's wort, you should counsel them and avoid any other serotonergic agents.
- **Linezolid.** We are using linezolid more often due to resistance. This is a monoamine oxidase inhibitor as well. Be cautious of using this in someone who is taking a lot of serotonergic agents. You could see serotonin syndrome with linezolid.