MISCELLANEOUS ANTIDEPRESSANTS
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Objectives

1. Understand the pathophysiology of the various antidepressants reviewed in this handout.
2. Become familiar with the clinical presentation of patients poisoned by the various antidepressants reviewed in this handout.
3. Develop a basic understanding of poison management of the various antidepressants reviewed in this handout.

I. SELECTIVE SEROTONIN REUPTAKE INHIBITORS

SSRIs inhibit the reuptake of serotonin at presynaptic terminals resulting in an increase in serotonergic activity at selected neuronal pathways in the CNS. There are various types of SSRIs available to treat depression with each possessing uniquely different pharmacological characteristics at therapeutic doses.

For the most part, SSRIs have a relatively low order of toxicity when compared to TCAs and MAOIs. Death due to SSRI poisoning alone is extremely rare. This is fortunate given that SSRI ingestions are now the most common form of antidepressant overdose.

Fluoxetine/Sertraline/Paroxetine

Clinical Features: The most common adverse effects following poisoning are nausea, vomiting, tremor, and a decreased level of consciousness. Seizures have been rarely reported with massive ingestions. Cardiotoxicity (tachycardia, bradyarrhythmias, conduction abnormalities) has been reported but usually in case reports in which other agents have been ingested concurrently.

II. OTHER ANTIDEPRESSANTS

Trazodone/Nefazodone

Clinical Features: The toxicity of these agents resemble that of fluoxetine and sertraline, however, profound sedation appears to be more commonly reported. Not only do these agents inhibit presynaptic serotonin reuptake, they also block 5-HT₂ receptors at the post-synaptic neuron. These agents are also block alpha₁-adrenergic receptors, which may result in hypotension, an uncommon clinical finding.

Various cases have reported a variety of adverse cardiac effects including, Torsades de Pointes preceded by QT interval prolongation, bradyarrhythmias, and ventricular arrhythmias. A causal role for trazodone in these cases is difficult to defend.

Venlafaxine (Effexor®)

Clinical Features: Venlafaxine is also described as a “bicyclic” antidepressant or “second generation cyclic antidepressant”. It is markedly less toxic than the tricyclic antidepressants but adverse cardiovascular effects have been reported. Tachycardia and hypertension may be attributed to its ability to block norepinephrine and dopamine reuptake in addition to serotonin reuptake. Seizures appear to be relatively more common with venlafaxine poisoning compared to the other SSRIs.
**Bupropion (Wellbutrin)**

**Clinical Features:** Bupropion is not an SSRI but should be mentioned when discussing antidepressant poisoning. The exact mechanism of action has not been clearly determined, but bupropion does appear to block the neuronal reuptake of dopamine and norepinephrine. Unlike SSRIs, seizures are commonly associated with bupropion overdose and may be life threatening. Other clinical manifestations of bupropion poisoning are relatively minor include lethargy, sinus tachycardia, and tremor. Deaths following large ingestions of bupropion alone are rare but have been reported.

- Toxic dose of buproprion is considered to be anything greater than 1.5X therapeutic. The usual therapeutic dose is 300 to 450 mg per day. Seizures may be seen with single acute doses greater than 600 to 900 mg.

**Mirtazapine (Remeron)**

Mirtazapine is a presynaptic alpha<sub>2</sub>-adrenoreceptor antagonist as well as a 5-HT<sub>2</sub> and 5-HT<sub>3</sub> antagonist. It enhances noradrenergic transmission by increasing noradrenergic cell firing and norepinephrine release. Given that this agent is relatively new, experience with overdose or poisoning is extremely limited. As with the SSRIs, mirtazapine appears to have a relatively low order of toxicity. Disorientation, drowsiness, amnesia, and tachycardia have been reported with overdose. Should mirtazapine begin to show significant potential to cause major complications in overdose, one must wonder whether a specific presynaptic alpha<sub>2</sub>-adrenoreceptor agonist such as clonidine may be a treatment alternative.

**SUGGESTED READING**