other antidepressant overdoses

SSRIs

General

- The SSRIs have a much more favorable side-effect profile than the TCAs, and overdoses are usually associated with little significant toxicity.
- Mortality due to SSRI overdose is very uncommon and in most reported cases has been associated with coingestion of other psychotropic agents, benzodiazepines, opiates, or alcohol
- Venlafaxine overdose is associated with the highest mortality rate among the SSRIs.
- The most common manifestations are lethargy, diaphoresis, nausea and vomiting, sinus tachycardia, and tremor. Seizures, serotonin syndrome (discussed later), cardiac conduction disturbances (including QRS and QT prolongation), and atrial and ventricular dysrhythmias occasionally have been reported.
- Although uncommon, the most serious toxic manifestation of the SSRIs is a constellation of symptoms and signs referred to as the serotonin syndrome

serotonin syndrome

clinical features:

Manifestation	% of Cases
Altered Mentation	
Confusion	41
Agitation	36
Coma	10
Lethargy/obtundation	7
Autonomic Dysfunction	
Diaphoresis	49
Tachycardia	44
Hyperthermia	27
Nausea/vomiting	27
Mydriasis	20
Diarrhea	10
Neuromuscular Hyperactivity	
Myoclonus	49
Hyperreflexia	41
Restlessness	29
Muscle rigidity	20
Tremor	17
Trismus	7

causes:
- Although it has been reported with a single agent, the serotonin syndrome almost always occurs in patients taking two or more drugs that increase 5-HT levels.
- The most commonly implicated drug combinations are an SSRI with a TCA and an SSRI with an MAOI.
- The serotonin syndrome has also been reported in patients receiving one or more medications that inhibit SSRI metabolism by the cytochrome P450 system.

differences compared to neuroleptic malignant syndrome:
- Neuroleptic malignant syndrome is perhaps the most commonly considered alternative diagnosis, because altered mentation and autonomic and neuromuscular dysfunction occur in both.
- Several important differences exist:
(i) neuroleptic malignant syndrome is an idiosyncratic reaction that usually develops after prolonged exposure to neuroleptic drugs or the withdrawal of dopamine receptor agonists.
(ii) unlike serotonin syndrome, the clinical manifestations of neuroleptic malignant syndrome usually develop gradually over days or weeks.
(iii) neuroleptic malignant syndrome usually is accompanied by marked hyperthermia, severe muscle rigidity, and rhabdomyolysis, but not by mydriasis, diarrhea, hyperreflexia, and myoclonus.
(iv) unlike serotonin syndrome, neuroleptic malignant syndrome is frequently associated with multiple organ failure, and death occurs in as many as 20% of patients.

treatment

General:
- The treatment of SSRI overdose is primarily supportive.
- Gastric lavage is almost never indicated, given the low risk of serious drug toxicity.
- Single-dose activated charcoal may be administered to patients who present within 1 hour after drug ingestion.
- Because major morbidity and mortality almost always result from the effects of other ingested medications, efforts must be made to identify and treat the toxic manifestations of these drugs.

Serotonin syndrome:
- Treatment of the serotonin syndrome is also largely supportive, although it is essential that all serotonergic agents be identified and discontinued. The serotonin syndrome usually has a benign course, and symptoms and signs typically resolve within 24 hours after discontinuation of the offending medications.
- Occasionally, however, severe complications occur and require specific therapy; these include marked hyperthermia, rhabdomyolysis, disseminated intravascular coagulation, renal failure, and acute respiratory distress syndrome.
- Case reports suggest that the serotonin receptor antagonists, cyproheptadine and chlorpromazine, may be useful in severe cases.

MAOIs

- The symptoms and signs that accompany MAOI overdose are believed to result primarily from a hyperadrenergic state produced by the inability to metabolize and inactivate NE in the central and peripheral nervous systems.

manifestations

- Clinical manifestations, which may be delayed for up to 24 hours, include mydriasis, flushing, diaphoresis, tachycardia, hypertension, hyperthermia, muscular rigidity, agitation, delirium, and seizures.
- Hypotension may occur later in the course, probably as the result of depletion of NE stores.

clinical course:

- Overdose with the irreversible MAOIs is commonly accompanied by life-threatening toxicity, and the mortality rate is similar to that of TCA ingestion.
- Reversible MAOIs, such as moclobemide, are much less toxic, and even massive overdoses have been accompanied by little morbidity.

management:

- Patients with MAOI overdose should undergo gastric lavage and receive activated charcoal, if they present within 1 hour after drug ingestion.
- Severe hypertension is best controlled with sodium nitroprusside, and hypotension usually responds well to NA.
- Dopamine acts largely by releasing stored NA and should be avoided, because it may either worsen the hyperadrenergic state or be ineffective due to endogenous NA depletion.
- Hyperthermia may be severe and may require evaporative cooling techniques.
- Muscle rigidity usually responds to benzodiazepines but may require the use of neuromuscular blockade.
- Seizures typically respond to benzodiazepines, phenytoin , and phenobarbital

atypical antidepressants

- Relatively little is known about the consequences of overdose with the atypical antidepressants.
- Large overdoses of bupropion can cause seizures and QRS prolongation, and rhabdomyolysis and hepatic necrosis have been reported.
- Mirtazapine ingestion has been accompanied by CNS and respiratory depression.
- Treatment of overdose with atypical antidepressants is largely supportive.