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 coningestion of other psychoactive agents, benzodiazepines, opiates, or alcohol. Venlafaxine overdose is associated with the highest mortality rate among the SSRIs.

The common manifestations are lethargy, diaphoresis, nausea and vomiting, sinus tachycardia, and tremor. Seizures, serotonin syndrome (discussed later), cardiac conduction disturbances (including ORS 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.

- 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.

- 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. 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. 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.

- Overdose with the irreversible MAOIs is commonly accompanied by life-threatening toxicity, and the mortality rate is similar to that of TCA ingestion.

- 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 antidepressants that inhibit SSRI metabolism by the cytochrome P450 system.

- Severe muscle rigidity, and rhabdomyolysis, but not by mydriasis, diarrhea, hyperreflexia, and myoclonus. Unlike serotonin syndrome, neuroleptic malignant syndrome is frequently associated with multiple organ failure, and death occurs in as many as 20% of patients.

- 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.