



Introduction

About 12.7% of Americans over the age of 12 are currently taking antidepressant medications, according to the National Center for Health Statistics for treatment of anxiety disorders or depression. The four most common antidepressant drug classes used to treat major depression are selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and monoamine oxidase inhibitors (MAOIs). Some patients also take these drugs to treat other illnesses such as chronic pain and low energy (Saraghi et al., 2018). Each of these drug classes has a unique effect on the body. In surgery, anesthesia will encounter patients on antidepressants every day. Some anesthetics, in combination with antidepressants, can have adverse effects on the patient and can affect the procedure's success. Thus, the anesthesia care provider must know the pharmacodynamics and pharmacokinetics of antidepressant drug classes and specific drug interactions between anesthetic drugs and antidepressants.

TABLE 25-1 ■ Characteristics of severe depression

Depressed mood
Markedly diminished interest or pleasure in almost all activities
Fluctuations in body weight and appetite
Insomnia or hypersomnia
Restlessness
Fatigue
Feelings of worthlessness or guilt
Decreased ability to concentrate
Suicidal ideation

SSRIs

With an SSRI overdose, serotonin syndrome can occur. Serotonin syndrome can be life-threatening and cause many adverse symptoms. It is rare for serotonin syndrome to occur by SSRIs themselves but usually happens in combination with other drugs (Stoelting, R. K., Hines, R. L., & Marschall, K. E., 2018). It has also been found that SSRIs can cause QT prolongation. SSRIs also possess some anti-inflammatory properties and have also been shown to decrease platelet function, leading to an increase in perioperative bleeding (Hemmings, Egan, 2019). SSRIs also have synergistic effects with other anticoagulants, thereby increasing the risk of bleeding complications (Saraghi et al., 2018).

TCAs

Long-term treatment with TCAs may also change the response to pancuronium, which has been associated with tachydysrhythmias. Ketamine, meperidine and epinephrine should also be avoided as they have been shown to produce tachydysrhythmias similar to pancuronium (Stoelting, R. K., Hines, R. L., & Marschall, K. E., 2018). Due to changes in norepinephrine uptake, TCAs may also exaggerate rebound hypertension after cessation of antihypertensive medication. In combination with volatile anesthetics, especially halothane, TCAs have been shown to increase the likelihood of arrhythmias. Centrally acting anticholinergic drugs should be avoided in combination with patients on TCAs because they can have additive anticholinergic effects (Hemmings, Egan, 2019).

SNRIs

SNRI use has many side effects, such as sedation, nausea, insomnia, tachycardia, sexual dysfunction, and anticholinergic effects. Due to the blocking of norepinephrine reuptake, high heart rates and high blood pressure are common. One of the SNRIs, Venlafaxine, inhibits CYP450 enzymes. Since SNRIs increase norepinephrine activity and impact adrenergic neurotransmission, epinephrine activity may be prolonged with exaggerated effects. Exaggerated cardiovascular effects are seen with indirect pressors as well. Like SSRIs, patients on SNRIs are also at an increased risk for perioperative bleeding due to the reduction of platelet levels of serotonin (Saraghi, et al, 2018).

MAOIs

Oral MAOI-A inhibits the breakdown of dietary amines and if a patient ingests food with tyramine, a serious hypertensive crisis can occur. For this reason, intense dietary restriction may be required. Since MAOIs irreversibly inhibit MAO, when combined with sympathomimetics, they can also cause a hypertensive crisis. In the operating room, many drugs can cause dangerous effects when combined with MAOIs. When combined with meperidine, which inhibits the reuptake of serotonin, serotonin syndrome may develop. Serotonin syndrome manifests first with hypertension, clonus, agitation, and hyperthermia which may progress to hypotension, hypoventilation, and coma. Many other opioids also inhibit serotonin reuptake which when combined with MAOIs can be associated with perioperative serotoninergic toxicity. (Hemmings, Egan, 2019). Some sources recommend cessation of the drug two to three weeks before elective surgery.

Drug Class	Tricyclic Antidepressants (TCAs)	Monoamine Oxidase Inhibitors (MAOIs)	Selective Serotonin Reuptake Inhibitors (SSRIs)	Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)
Medications	Amitriptyline (Elavil®) Desipramine (Norpramin®) Doxepin (Sinequan®) Imipramine (Tofranil®) Nortriptyline (Pamelor®) Many Others	Isocarboxazid (Marplan®) Phenelzine (Nardil®) Tranylcypromine (Parnate®)	Citalopram (Celexa®) Escitalopram (Lexapro®) Fluoxetine (Prozac®) Fluvoxamine (Luvox®) Paroxetine (Paxil®) Sertraline (Zoloft®)	Desvenlafaxine (Pristiq®) Duloxetine (Cymbalta®) Levo-milnacipran (Fetzima®) Milnacipran (Savella®) Venlafaxine (Effexor®)

Conclusion

For each class, serotonin syndrome needs to be at the forefront of the provider's mind. When a patient is on selective serotonin reuptake inhibitors (SSRIs), anesthesia should be aware of possible QT prolongation and the antiplatelet effects. With TCAs, pancuronium, ketamine, and some volatile anesthetics should be avoided. For tricyclic antidepressants (TCAs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs), adverse interactions with sympathomimetics can occur. For monoamine oxidase inhibitors (MAOIs) the patient's blood pressure and heart rate should be tightly controlled to prevent the need to administer sympathomimetics or vasopressors. Many opioids such as meperidine should be avoided in patients taking MAOIs due to the high risk of serotonin syndrome.

References

Saraghi, M., Golden, L., & Hersh, E. V. (2018). Anesthetic considerations for patients on antidepressant therapy—part II. *Anesthesia progress*, 65(1), 60-65; Butterworth, J. F., Mackey, D. C., & Wasnick, J. D. (2018). *Morgan & Mikhail's clinical anesthesiology*. New York: McGraw-Hill Education; "Antidepressant Drugs." *Pharmacology and Physiology for Anesthesia: Foundations and Clinical Application*, by Hugh C. Hemmings and Talmage D. Egan, Elsevier, Inc., 2019; Sajan, F., Conte, J. V., Tamargo, R. J., Riley, L. H., Rock, P., & Faraday, N. (2016); Hines, R. L., & Marschall, K. E. (2018). *Stoelting's anesthesia and co-existing disease*. Philadelphia, Pa: Elsevier.