

Clonidine Overdoses

Clonidine is a centrally acting alpha-2 adrenergic agonist that is approved for the management of hypertension, attention-deficit hyperactivity disorder (ADHD) and as adjunctive therapy for management of cancer pain. Off-label uses include ethanol and opioid withdrawal, smoking cessation, hot sweats, and adjunctive therapy for postoperative pain. Clonidine is also abused for its sedative effects, to enhance the effects of opioids, or to self-treat opioid withdrawal. Clonidine stimulates both alpha2-adrenoceptors and imidazoline receptors in the brain, which reduces sympathetic outflow leading to a decrease in peripheral resistance, renal vascular resistance, heart rate, and blood pressure.

Clonidine is available as immediate release and extended release tablets as well as transdermal patches. Clonidine is also an ingredient in some compounded creams used topically for pain. Peak serum concentrations occur within 1-2 hours after immediate release and at close to 8 hours with extended release formulations. The transdermal formulation reaches maximal plasma concentrations within 2-3 days of application. Half-life ranges from 5-20 hours.

Overdoses occur because of unintentional oral ingestions by children, therapeutic errors, and intentional overdoses in adolescents and adults. There are case reports of serious toxicity resulting from unintentional ingestion or inappropriate dermal application of compounded creams and patches. Even discarded clonidine patches contain significant amounts of drug and are a danger to children. In a case series of pediatric clonidine ingestions, serious toxicity (coma, respiratory depression and hypotension) occurred with doses as low as 0.3 mg; however, an earlier report found that as little as one 0.1 mg tablet caused toxicity (*J Pediatr* 2005;146:263-6; *Vet Hum Toxicol* 1990;32:220-3). In contrast, a recent study of acute clonidine overdoses in adults found persistent bradycardia and CNS depression but concluded that toxicity was not life threatening. (*Clin Toxicol* 2017;55:187-92).

Toxic effects usually occur within 30 minutes to 4 hours of exposure and resolve within 24-72 hours. Tachycardia and hypertension may be present early on and usually progress to bradycardia and hypotension. Other clinical effects include lethargy, coma, seizures (rare), hypotonia and hyporeflexia, miosis, respiratory depression and apnea, and hypothermia. Cardiac dysrhythmias such as AV block may occur.

Following an oral overdose, consider administering activated charcoal if soon after the ingestion and the patient is able to protect the airway. If a clonidine patch is present on the skin, remove it and wash the exposed area. Patients may require respiratory and blood pressure support. Bradycardia can be treated with atropine. The role of naloxone to reverse clonidine-induced respiratory depression, hypotension, and coma is unclear. In some studies, over 50% of cases demonstrated some response, but in others, few or no patients responded to naloxone.



Did you know?

There are other drugs that act like clonidine and produce similar toxicity.

Guanfacine, an anti-hypertensive (immediate release) and ADHD medication (extended release), has a long half-life sometimes resulting in delayed and prolonged toxicity. The skeletal muscle relaxant tizanidine has a short half-life so duration of toxicity may be shorter than clonidine. Imidazoline topical decongestants (e.g. tetrahydrozoline in eye drops and oxymetazoline in nose drops) can result in toxicity with ingestion of as little as 1-2 milliliters. All of these medications have similar pharmacologic activity as clonidine and, therefore, produce similar toxicity.

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