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## Benzodiazepines (Part 2)

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### Uses

Therapeutically, Benzodiazepines are an important part of medical treatment when used judiciously and appropriately prescribed by a physician. They have hypnotic, anxiolytic, anticonvulsant, amnestic and muscle relaxant properties. They are often used for short-term relief of severe, disabling anxiety or insomnia, are the drug of choice to detoxify patients from alcohol, are used for status epilepticus, and are a mainstay in the emergent treatment of psychiatric patients in the Emergency Room.

Consideration of how long they stay in the body has been important. Treatment of insomnia is best through short acting benzodiazepines that minimize the next morning hang-over; whereas the treatment of anxiety is more served by those with long half-lives in the body that maintain a relatively constant blood level. Versed (midazolam) is one of the shortest acting benzodiazepines and is commonly used with an opiate for twilight sedation during surgical or endoscopic procedures where once the procedure is over, the patient needs to be quickly revived.

### Side-effects

Benzodiazepines have replaced the barbiturates because of their ubiquitous availability, lower abuse potential, lower toxicity and relatively lower adverse reactions and interactions. Still, drowsiness, ataxia, confusion, vertigo

(medical), impaired judgement, and a number of other effects are common which place the person at risk of accidents while driving vehicles or operating machinery, in addition to falls. As mentioned, the grave risk of additive sedation and respiratory depression in combination with other CNS depressants, in particular opiates and alcohol, place the user at high risk of death. The effects of long-acting benzodiazepines can also linger over to the following day continuing to place the user at risk.

The antidote for all benzodiazepine intoxication is Annexate (flumazenil), the specific benzodiazepine antagonist. This can be used with caution in patients presenting with unexplained loss of consciousness in emergency room setting; however that runs the risk of precipitating a seizure.

### Abuse and Dependence

Benzodiazepines induce physical dependence and are potentially addictive. An abrupt discontinuation of benzodiazepines is one of the few withdrawal syndromes that can cause death. Hence, every person on long-term or high dosage of any benzodiazepine should be carefully weaned off the drug, and most of the time, under medical supervision in a detox unit. A common method substitutes phenobarbital for the benzodiazepine which is then tapered down.

Onset of the withdrawal syndrome might be delayed by days or a week in the case of the long acting benzodiazepines or may present soon after the last

dose or sudden reduction, as in the case of Xanax (Alprazolam), and placing the person at extreme risk of having seizures.

The benzodiazepine withdrawal syndrome is characterized by:

- Insomnia
- Anxiety
- Panic
- Tremor
- Perspiration
- Loss of appetite
- Muscle aches and cramps
- Nausea
- Vomiting
- Urinary retention
- Sensitivity to light/sound
- Paresthesia's (can be described as tingling, crawling, needle-like, or stabbing)
- Nightmares or hyper vivid dreams
- Disassociation
- Disorientation
- Delirium

Post-acute withdrawal symptoms can last up to a year. Some of the withdrawal symptoms are identical to the symptoms for which the medication was originally prescribed. Benzodiazepines are valued by many patients for their ability to ameliorate existing conditions, while benzodiazepine dependency can cause them. A Canadian case-controlled study of 8980 elderly people performed in 2014 demonstrated a relationship between benzodiazepine use and the development of Alzheimers. Their study showed a 43-51% increase in risk.<sup>3</sup>

Part 3 of this article will appear in the January issue of Toxicology Times.