BEYOND THE BASICS

Tranquillizers & Sleeping Pills

What are tranquillizers and sleeping pills?

Tranquillizers and sleeping pills – also called anxiolytics, sedatives and hypnotics – are all central nervous system (CNS) depressants. The clinical designation of a particular medication is determined by its chemical structure and pharmacokinetic profile. They are all able to induce depression of specific cognitive and behavioural functions.[1]

CNS depressants of this type can be divided into three chemical groups:

- Barbiturates, such as mephobarbital (Mebaral®) and sodium pentobarbital (Nembutal®), were developed to treat sleep problems, anxiety, tension, high blood pressure and seizures. Because of their highly addictive nature and risks associated with overdose, they are now less widely used.
- Benzodiazepines, such as diazepam (Valium®), alprazolam (Xanax®) and estazolam (ProSom®), can be prescribed to treat anxiety, acute stress reactions, panic attacks, convulsions and sleep disorders. They are often prescribed instead of barbiturates; however, they are intended to be a relatively short-term solution for patients.
- Nonbenzodiazepines, such as zolpidem (Ambien®), zaleplon (Sonata®) and eszopiclone (Lunesta®), are newer sleep medications commonly prescribed to treat sleep disorders. These medications are becoming more popular because they may offer a lowered risk of abuse and addiction.[2]

Any of the barbiturates and benzodiazepines have the potential for misuse or abuse due to the desired effects they provide to the user. A sense of well-being, relaxation, sleepiness and even euphoria can be achieved. Unfortunately, it is not uncommon for individuals to use depressants in combination due to the synergistic effect this will yield.[3]

Common street names for prescription tranquillizers and sleeping pills include tranks, reds, yellows, blues, ludes, barbs, downers, Vs (Valium®), red birds, red devils, yellow jackets, blue heavens, Christmas trees and rainbows.

Medical Use

Depressants within this group are commonly prescribed to treat anxiety disorders and thus reduce feelings of both acute and chronic anxiety, panic and stress. They are also used to induce sleep and resolve insomnia. Additionally, they may be prescribed to address muscle spasms, involuntary movement disorders, seizures and detoxification from alcohol.[4]

Benzodiazepines specifically produce a sense of calm and well-being at low doses and are commonly prescribed for management of anxiety. The clinical use of barbiturates includes treatment of epileptic seizures, alleviation of migraine headaches and induction of general anesthesia.[1]

Prevalence of Use

In Canada, comprehensive information regarding abuse of prescription drugs is generally not available; however, a research review prepared by the Canadian Centre on Substance Abuse (CCSA) was noteworthy in identifying that adolescents, older adults, women and Aboriginal people have an increased risk of abusing prescription drugs. Previous illicit drug use is also an indicator of potential abuse of prescription drugs.[5]

The Canadian Alcohol and Drug Use Monitoring Survey conducted in 2008 by Health Canada queried participants on the use and abuse of three classes of psychoactive pharmaceutical drugs: opioid pain relievers, stimulants, and tranquillizers and sedatives.[6] In this survey, one in ten Canadians (10.7%) reported the use of sedatives or tranquillizers in the past 12 months. Only 1.4% of these users reported the use of sedatives to get high. When sedatives and tranquillizers were used to get high, there were no differences among the users according to sex or age.[6]

Pharmacokinetics

The rate at which drugs are absorbed, metabolized and excreted varies, depending on the nature of the drug itself, as well as factors such as the user's physical build, gender, age, health and genetics. For the benzodiazepines, research has shown that seniors and individuals with poor liver function are unable to metabolize these compounds at the same rate as a younger, healthier person. Therefore, in older adults the half-life of the benzodiazepine may be twice as long as would normally be expected, resulting in prolonged psychomotor slowing.[4,7]

There is wide variation in the rate of onset and offset for both benzodiazepine and barbiturate classes of CNS depressants. Differences in onset and duration of action for specific medications depend largely on the rates at which they are metabolized and eliminated from the body. For example, the half-life for triazolam (Halcion®) is only two to five hours, while the half-life of diazepam is 20 to 100 hours, and that of an active metabolite of diazepam (desmethyldiazepam) is 36 to 200 hours. With repeated daily dosing, high concentrations can build up in the fatty tissues of the body.[8]

Furthermore, the duration of action is usually considerably less than the half-life. With most benzodiazepines, patients will notice the effects usually wear off within a few hours; however, as the drug is still present, it continues to exert subtle effects within the body or may become apparent during continued use and may contribute to withdrawal symptoms when dosage is reduced or stopped.[8]

Barbiturates, like benzodiazepines, differ from each other primarily in terms of how quickly the drugs act and the intensity and duration of action. These differences are the main consideration in deciding for what purposes these drugs will be used.[1]

Pharmacodynamics

As CNS depressants, barbiturates and benzodiazepines enhance the actions of the neurotransmitter gamma-aminobutyric acid (GABA), resulting in decreased brain activity. Although different classes of CNS depressants work in unique ways, it is ultimately their common ability to increase GABA activity that produces a drowsy or calming effect.[2]

While benzodiazepines or barbiturates produce similar effects as a result of their impact on GABA activity, the effects are generated due to different processes. Barbiturates increase the duration of opening of the chloride ion channel at the GABAA receptor, resulting in increased effectiveness of GABA. It is this direct access, or gating of the chloride ion channel, that can result in higher toxicity than would result from benzodiazepine use and increase risk of overdose. Benzodiazepines increase the frequency of opening of the chloride ion channel at the GABAA receptor, resulting in increased potency of GABA.[9]

Short-term Effects

Short term effects of benzodiazepines include a feeling of well-being, loss of inhibition, decreased muscle tension, reduced mental alertness and mildly impaired coordination and balance. On rare occasions, and usually at high doses, paradoxical reactions such as rage, personality changes and sleep disturbances can occur. Side effects such as skin rashes, nausea and dizziness have been reported. Benzodiazepines prescribed as sleep aids may produce withdrawal symptoms commonly referred to as "hangover" effects.

Small doses of barbiturates relieve tension; large doses produce drowsiness, staggering, blurred vision, impaired thinking, slurred speech, impaired perception of time and space, slowed reflexes and breathing, and reduced sensitivity to pain.

Long-term Effects

Some benzodiazepines that are eliminated slowly (such as diazepam) accumulate in body tissues during sustained use. Chronic abuse of benzodiazepines may result in: impairment in thinking, short-term memory and judgment; confusion and disorientation; depression and impaired physical coordination. Prolonged use may also lead to increased, rather than reduced, aggressiveness in some people. Suicidal ideations may also be present.[10]

Long-term, high-dose use of barbiturates may result in impaired vision, memory and judgment, slurred speech, as well as depression or mood swings. Changes in liver function may result in faster metabolism of other drugs.[10]

Toxic Effects

Despite their beneficial effects for people suffering from anxiety or sleep disorders, barbiturates and benzodiazepines can be addictive.

CNS depressants should not be combined with any medication or substance that causes drowsiness, including prescription pain medicines, certain over-the-counter cold and allergy medications, and alcohol. If combined, the effect can be dangerously intensified, resulting in severe intoxication, unconsciousness, coma and death.[1,10]

Overdose with barbiturates can cause unconsciousness, coma and death. In the past, many of the deaths due to drugs (excluding alcohol) in Canada were caused by barbiturates and barbiturate-like drugs.[1,10]

Tolerance and Dependence

Tolerance to the sedative action of benzodiazepines, but not the anxiety-relieving effects, can develop with regular use over a few months, as can psychological and physical dependence.[10]

Regular use of barbiturates induces tolerance, making increased doses necessary to produce the desired effect. With barbiturates, tolerance develops more quickly to the mood-altering effects than to the effects on the respiratory system. As a result, an individual may increase their dosage to obtain the desired altered mental state; however, their respiratory system cannot handle the required increased dosage to accomplish this. Thus, the margin of safety between an effective dose and a lethal dose gradually narrows.[10]

Psychological dependence can occur with regular use of barbiturates, as can physical dependence.[10]

Withdrawal

Withdrawal from benzodiazepines can be problematic, although it is rarely life threatening. Withdrawal from prolonged use of other CNS depressants can have life-threatening complications. Therefore, someone who is thinking about discontinuing CNS depressant therapy or who is suffering withdrawal from a CNS depressant should speak with a physician or seek other medical treatment.[11]

Because all CNS depressants work by slowing the brain's activity, when an individual stops taking them the brain's activity can rebound and race out of control, possibly leading to seizures and other harmful consequences.[11]

Stopping use abruptly may result in withdrawal, which can include symptoms such as sleep disturbances, headache, tension, difficulty concentrating, trembling, anxiety and feeling tired. During withdrawal from very high doses of benzodiazepines, there is a risk of seizures, depression, paranoia, agitation and delirium. Withdrawal symptoms may be greater for benzodiazepines that are eliminated rapidly from the body.[10]

Withdrawal symptoms from barbiturates include restlessness, anxiety, insomnia, delirium and seizures and may result in death.[10]

Legal Issues

In Canada, barbiturates and benzodiazepines are governed by the provisions of the *Controlled Drugs and Substances Act* (CDSA) applicable to Schedule IV. This means individuals may have the prescribed drug in their possession, for their own use only. Trafficking, possession for the purpose of trafficking, possession for the purpose of exporting, production, import and export offenses are punishable on summary conviction by imprisonment for up to one year or on indictment by imprisonment for up to three years.[12]

It is also an offense under the CDSA for someone to obtain, or try to obtain, a controlled substance from a practitioner without disclosing all other controlled substances obtained from other practitioners within the previous thirty days.[12]

As well, the Criminal Code of Canada contains offenses related to driving while impaired by alcohol or other drugs. Manitoba has also enacted legislation to address drug-impaired driving.

Risks & Other Harms

Abusers of barbiturates and/or benzodiazepines who inject the drug expose themselves to additional risks, including contracting human immunodeficiency virus (HIV), hepatitis B and C and other blood-borne viruses.

As is the case in any abuse of licit and illicit drugs, there are potential adverse consequences related to the law, a person's financial situation, family relationships, and generally putting oneself at risk by participating in unsafe behaviours while under the influence of these drugs.[4]

Abuse of tranquillizers and/or sleeping pills can result in personality disturbances, learning problems, loss of memory and mental health problems.

Pregnancy & Lactation

When barbiturates and benzodiazepines are used by pregnant women, they cross the placenta and are distributed to the fetus. After birth, babies exposed to either drug in the uterus may show withdrawal symptoms.[4]

Late third trimester use and exposure during labour seems to be associated with much greater risks to the fetus. Some of these infants exhibit either hypotonia (floppy infant syndrome) or significant neonatal withdrawal symptoms. Symptoms – lasting for periods of hours to months after birth – vary from mild sedation, severely reduced muscle tone and reluctance to suck, to apnoeic spells, cyanosis and impaired metabolic responses to cold stress.[13]

Both barbiturates and benzodiazepines are excreted in breast milk. It is not recommended that mothers who use these medications breastfeed.[4]

Interventions

Ideally, special attention should be given to a patient's past or present involvement with substances prior to prescribing any controlled substance that is highly addictive. Good patient-doctor communication is an essential risk management approach for all prescription drugs, including tranquillizers and sleeping pills. A comprehensive medical history puts physicians in the best position to determine appropriate pharmaceutical interventions.[6]

Patients dependently involved with barbiturates and benzodiazepines should not attempt to stop taking them on their own, as withdrawal from these drugs can be dangerous and potentially life-threatening. Treatment can also involve detoxification, including rapid detoxification techniques, and traditional behaviour-oriented therapies, such as individual counselling, group or family therapy, contingency management and cognitive-behavioural therapies.[2]

Any treatment strategy used with those abusing prescription drugs must take into account the specific needs of the individual, as well as the particular substance being abused. This principle is the same for treatment of those who abuse both legal and illegal substances. Often the abuse of barbiturates and benzodiazepines occurs in conjunction with the abuse of another substance, such as alcohol or cocaine. In these cases of poly-drug abuse, the treatment approach must address the multiple dependencies.[10]

Substance Use & Mental Health

- Substance use and mental health problems can often occur together. This is commonly referred to as a co-occurring disorder.
- Substance use may increase the risk of mental health problems.
- People with mental health problems are at higher risk of developing substance abuse problems:
  - Sometimes they use alcohol and other drugs in an attempt to relieve themselves from mental health symptoms.
  - For most people alcohol and other substance use only covers up the symptoms and may make them worse.

Remember: A person's experience with any drug can vary. Here are a few of the many things that may affect the experience: the amount and strength of the drug taken, the setting, a person's mood and expectations before taking the drug, gender, overall health, past experience with that drug and whether more than one drug is being used at the same time. Using alcohol and other drugs at the same time can also be dangerous.

Sources

1. Cleveland State University. *Central Nervous System Depressants,* Academic Server. Available at http://www.academic.csuohio.edu/eingersoll/778ac1.htm (accessed February 2010).
2. National Institute on Drug Abuse. *Prescription and Over-the-Counter Medications Fact Sheet,* 2009. Available at www.drugabuse.gov/PDF/Infofacts/PainMed09.pdf (accessed February 2010).
3. Fandrey, S. L. *Applied Aspects of Pharmacology,* Addictions Foundation of Manitoba, 2005.
4. Longo, L. P. & Johnson, B. "Addiction: Part 1. Benzodiazepines – side effects, abuse risk and alternatives," *American Academy of Family Physicians,* 2000. Available at http://www.aafp.org/afp/20000401/2121.html (accessed February 2010).
5. Weekes, J., Rehm, J. & Mugford R. *Prescription Drug Abuse FAQ,* Canadian Centre on Substance Abuse (CCSA), 2007. Available at http://www.ccsa.ca/2007%20CCSA%20Documents/ccsa-011519-2007.pdf (accessed February 2010).
6. Health Canada. *Canadian Alcohol and Drug Use Monitoring Survey, Summary Results for 2008*. Available at http://www.hc-sc.gc.ca/hc-ps/drugs-drogues/stat/_2008/summary-sommaire-eng.php (accessed February 2010).
7. Addictions Foundation of Manitoba (AFM). *Facts on Drugs,* 2004.
8. Ashton, H. *Benzodiazepines (Valium, Sobril. Xanax, Xanor, Mogadon, Rohypnol, etc.) Half Life (Duration of effect),* Web4Health, 2008. Available at http://web4health.info/it/bio-benzo-overview.htm
9. World Health Organization (WHO). *Neuroscience of Psychoactive Substance Use and Dependence,* Geneva, 2004.
10. Health Canada. *Straight Facts About Drugs and Drug Abuse,* 2000. Available at http:///www.hc-sc.gc.ca/hc-ps/pubs/adp-apd/straight_facts-faits_mefaits/index-eng.php
11. Drug Addiction Treatment Center. *What are CNS depressants?* 2003. Available at http://www.drug-addiction.com/cns_depressants.htm
12. Health Canada. *Straight Facts About Drugs and Drug Abuse – What are Canada's Drug Laws?* 2009. Available at http://www.hc-sc.gc.ca/hc-ps/pubs/adp-apd/straight_facts-faits_mefaits/drug_laws-lois_de_drogues-eng.php (accessed March 2010).
13. National Center for Biotechnology Information. *The Effects of Benzodiazepine During Pregnancy and Lactation,* 1994. Available at http://www.ncbi.nlm.nih.gov/pubmed/7881198

The Addictions Foundation of Manitoba (AFM) offers a broad range of prevention and treatment services for alcohol, other drugs and gambling. These are designed to meet the needs of all Manitobans and include harm reduction and abstinence-based programs.

For more information, contact your local AFM office or visit our website: www.afm.mb.ca.

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