

NSW Health

Drug Compendium:

Supplement Reference for AOD Treatment



Drug Compendium

The Drug Compendium should be referred to in conjunction with the following policy, guidelines and standards:

- PD2020_032: Nursing and Midwifery Management of Drug and Alcohol use in the Delivery of Health Care
- Drug and Alcohol Withdrawal Clinical Practice Guidelines
- Clinical Guidelines for the Management of Substance Use During Pregnancy, Birth and the Postnatal Period
- Opioid Overdose Response and Take-Home Naloxone Policy
- Australian Health Practitioner Regulation Agency (AHPRA) Nursing and Midwifery Board: Standards for Practice

Table of contents

Alcohol

Opioids

Benzodiazepines and 'Z drugs'

Psychostimulants

Cannabis

Nicotine

Hallucinogens

Inhalants and solvents

Ketamine

Gamma hydroxybutyrate (GHB)

Androgenic anabolic steroids (AAS)

Emerging drugs of concern

NSW Ministry of Health
1 Reserve Road
ST LEONARDS NSW 2065
Tel. (02) 9391 9000
Fax. (02) 9391 9101
TTY. (02) 9391 9900
www.health.nsw.gov.au

This work is copyright. It may be reproduced in whole or in part for study or training purposes subject to the inclusion of an acknowledgement of the source. It may not be reproduced for commercial usage or sale. Reproduction for purposes other than those indicated above requires written permission from the NSW Ministry of Health.

The NSW Ministry for Health acknowledges the traditional custodians of the lands across NSW. We acknowledge that we live and work on Aboriginal lands. We pay our respects to Elders past and present and to all Aboriginal people.

Further copies of this document can be downloaded from the NSW Health webpage: www.health.nsw.gov.au

© NSW Ministry of Health 2021

SHPN (CAOD) 210429
ISBN 978-1-76081-751-0

May 2021

Alcohol

Overview

Many Australians drink alcohol at levels that cause few adverse effects. However, some drink at levels that increase their risk of alcohol-related harms, significant ill health and hardship. Alcohol-related harm to health is not limited to drinkers but also affects families, bystanders and the broader community. In Australia, alcohol is the second leading cause of drug-related death and hospital admissions after tobacco.

Alcohol is a CNS depressant that affects almost all of a person's cells and systems.

Current usage

The proportion of Australians aged 14 or older who consumed alcohol daily declined between 2013 (6.5%) and 2016 (5.9%). In the 12 months to 2016, 77.5% of Australians had reported consumption of alcohol.

Effects and presentation

Apart from physiological effects, alcohol consumption on a single occasion (depending on the amount) increases the risk of accidents, misadventures and injuries during and immediately after drinking. Young people are particularly susceptible to adverse alcohol-related events, including road injury (in a vehicle or as a pedestrian), suicide, assaults and drowning.

Acute effects (mild intoxication)

Immediate effects of alcohol are on the brain, beginning with feelings of relaxation, wellbeing and loss of inhibitions. As the intake of alcohol increases, less pleasant effects include drowsiness, dizziness, loss of balance and coordination, headaches, nausea and vomiting, blurred vision, slurred speech and dry mouth.

Long-term effects

Alcohol dependence: brain damage and problems with brain development; malnutrition; cardiovascular problems; cancer – alcohol has been linked to a range of cancers (e.g. including mouth, oesophagus, liver and breast cancers); liver problems; increased risk of mental health problems such as anxiety and depression; may increase problems with diabetes and obesity.

Alcohol use is associated with increased rates of suicide attempts and completed suicides.

Wernicke-Korsakoff refers to two different syndromes, each representing a different stage of the disease. Wernicke encephalopathy (WE) is an acute syndrome requiring emergent treatment to prevent death and neurologic morbidity. Korsakoff syndrome (KS) refers to a chronic neurologic condition that usually occurs because of WE.

Signs and symptoms of WE include:

- encephalopathy – characterised by profound disorientation, indifference and inattentiveness
- oculomotor dysfunction – nystagmus or reduced eye movement
- gait ataxia – ataxia that primarily involves stance and gait and is likely due to a combination of polyneuropathy, cerebellar involvement and vestibular dysfunction.

WE is initially reversible if recognised and treated with parenteral vitamin B1 (thiamine). Untreated, WE can lead to KS, hypotension, hypothermia, permanent brain damage, coma and death. WE may be precipitated by administration of intravenous glucose solutions to individuals with thiamine deficiency. In susceptible individuals, glucose administration should be preceded or accompanied by thiamine administration.

Drug interactions

Alcohol may interact with a range of medications and illicit substances and can increase their potential for adverse effects or reduce their effectiveness. The effects of combining alcohol and drugs depend on the type and dosage of medication, the volume of alcohol consumed, and on personal factors such as genetics, gender and comorbid health conditions.

Commonly prescribed classes of medications such as benzodiazepines, opioids, analgesics, antipsychotics, antidepressants, certain antibiotics (e.g. metronidazole, tinidazole), antihistamines, anti-inflammatories and hypoglycaemic agents have known interactions with alcohol.

People treated for alcohol dependence may be taking disulfiram, which may lead to lethal outcomes if consumed with alcohol during treatment.

Alcohol

Intoxication and overdose

Alcohol intoxication is a potentially lethal condition. The majority of overdoses are due to polydrug toxicity involving the concomitant consumption of other CNS depressants, most commonly alcohol and benzodiazepines. Just as with other drugs, people can overdose on alcohol; death is usually due to respiratory depression or inhalation of vomitus. Each person has a different tolerance to alcohol - on average, the lethal blood alcohol concentration is 0.45-0.5%.

Signs of intoxication and overdose

Passing out or blackouts; stupor or coma; cold and clammy skin; lowered body temperature; lowered blood pressure; slow and noisy respiration; accelerated heart rate or bradycardia; strong smell of alcohol; positive breath alcohol reading.

Management of intoxication and overdose

Management of acute intoxication requires recognition and exclusion of other potential causes of changes in mental status, such as head trauma, hypoglycaemia, hypoxia, and poisoning with other agents. Treatment is largely supportive and consists of identification and correction of hypovolaemia and hypoglycaemia, close monitoring of respiratory status, and intravenous thiamine in patients at risk of WE.

Symptoms and onset of withdrawal

Severe alcohol withdrawal is potentially life-threatening. It is important to anticipate when it may occur and to suspect it when an unexplained acute organic brain syndrome is detected. Withdrawal can occur when the blood alcohol level is decreasing, even if the patient is still intoxicated. Consumption of benzodiazepines or other sedatives may delay the onset of withdrawal.

Onset of alcohol withdrawal is usually 6-24 hours after the last drink. In some severely dependent drinkers, simply reducing the level of consumption may precipitate withdrawal, even if they have consumed alcohol recently. Usually, withdrawal is brief, and resolves after 2-3 days without treatment; occasionally, withdrawal may continue for up to 10 days.

Alcohol withdrawal is a syndrome of CNS hyperactivity characterised by symptoms that range from mild to severe. Symptoms include sweating, anxiety, fever, tachycardia, tremor, nausea, vivid dreams, insomnia, hallucinations, delirium, hypertension, vomiting, dyspepsia and seizures.

Alcohol withdrawal delirium (previously referred to as Delirium Tremens or the 'DTs') is rare and is a diagnosis by exclusion. It is the most severe form of alcohol withdrawal syndrome, and a medical emergency. It usually develops 2-5 days after stopping or significantly reducing alcohol consumption. The usual course is 3 days but can be up to several weeks. Its clinical features are: confusion and disorientation; extreme agitation or restlessness - the patient often requires restraining; gross tremor; autonomic instability (e.g. fluctuations in blood pressure or pulse); disturbance of fluid balance and electrolytes, hyperthermia; paranoid ideation, typically of delusional intensity; distractibility and accentuated response to external stimuli; hallucinations affecting any of the senses, but typically visual (highly coloured, animal form).

Opioids

Overview

Opioids, used medically for pain relief, have analgesic and CNS depressant effects. The potential to cause euphoria is an effect that can lead to non-medical use.

Opioids can be divided into: opiates including morphine and codeine (consisting of alkaloid compounds occurring naturally in the opium poppy); semi-synthetic opioids including heroin, oxycodone and hydrocodone; and synthetic opioids including fentanyl, tramadol, and methadone. Common routes of recreational use include oral, intravenous injection, snorting and smoking.

Pharmacology

Opioids act mainly at mu-opioid receptors in the CNS, which reduces transmission of the pain impulse and modulates the descending inhibitory pathways from the brain. Activation of mu receptors in the CNS results in responses such as respiratory depression, analgesia, euphoria and miosis. Stimulation of peripheral mu-opioid receptors, in smooth muscle of the bronchi and intestines, results in cough suppression and opioid-induced constipation.

Examples seen in Australia

Heroin is an illicit opioid. Non-medical use of pharmaceutical opioids has been of increasing concern, in particular highly potent opioids such as oxycodone, hydromorphone and fentanyl. Stronger agents not used therapeutically for humans may be obtained online.

Current usage

In 2016, around 1 in 10 (11%) Australians aged 14 years and over had ever used at least one type of opioid for illicit or non-medical purposes, and 3.6% had used prescription opioids for non-medical purposes in the 12 months to 2016. Pharmaceutical opioids were responsible for more opioid deaths and poisoning hospitalisations than heroin. Strong opioids (e.g. morphine, oxycodone and fentanyl) accounted for 59% of all opioid prescriptions dispensed in 2016–17, of which oxycodone was the most commonly dispensed opioid prescription. Heroin use is relatively low, with 0.2% reporting use in the 12 months to 2016.

Suicide is a major clinical issue. Lifetime prevalence of attempted suicide is 14 times the general population for heroin users, accounting for 5–10% of heroin user deaths. An attempt is a strong predictor of subsequent attempts and completion.

Effects and presentation

Patients who have developed tolerance to opioids may show no acute effects after use of the drug at a dose typical for that patient. They may not be presenting for treatment of their addiction, but when hospitalised for other reasons may show signs of opioid withdrawal.

Acute effects (mild intoxication)

Reduced sensitivity to pain, euphoria or negative mood, dizziness or faintness, tiredness, confusion, restlessness, stiff muscles, constipation, dry mouth, stomach-ache and nausea, sweating, flushing and itching.

Long-term effects

Constipation, bloating and abdominal pain, irregular periods and infertility, reduced libido, damage to vital organs, tolerance, dependence, opioid-induced hyperalgesia, overdose and trauma. If injecting drugs, there is an increased risk of infection and vein damage. The injection of tablet or oral preparations may cause chronic passive vascular congestion of the liver and peripheral oedema. Heroin smoking ('chasing') is associated with impaired pulmonary function.

Opioids

Drug interactions

Combining opioids with stimulants such as ice, speed and ecstasy puts enormous strain on the heart and kidneys and increases the risk of overdose.

Taking substances that cause CNS and respiratory depression, (e.g. benzodiazepines, pregabalin, gabapentin and alcohol) with an opioid increases the risk of these effects (deaths have occurred); avoid combinations if possible or monitor closely if used together.

Opioid antagonists such as naloxone and naltrexone will reverse the effects of opioids and may precipitate withdrawal. Strongly binding partial agonists such as buprenorphine and buprenorphine/naloxone combinations may result in reduced effect of opioids.

Concurrent use of certain opioids with lithium and serotonergic agents may increase risk of serotonin syndrome.

Patients with increased tolerance to opioids, including those on Opioid Agonist Treatment

Increased tolerance to opioids reduces the analgesic effects of opioid pain relievers. Patients most likely to have increased tolerance include:

- patients who have been on regular prescribed opioids for long periods
- patients currently receiving opioid agonist treatment (OAT) - refer to NSW Clinical Guidelines: Treatment of Opioid Dependence 2018
- those who regularly take liver enzyme-inducing drugs (e.g. alcohol, some anticonvulsant medicines and anti-retroviral medicines).

For patients receiving OAT, analgesia should not be withheld unless medically indicated. Effective pain management starts with the dose usually required for an opioid naive individual, and then titrating doses upwards until adequate pain relief is achieved.

Intoxication and overdose

Risk factors for accidental overdose include history of overdose; frequent use and higher levels of dependence; use following period of abstinence (due to a reduced level of tolerance); mixing drugs (e.g. benzodiazepines, cocaine and pregabalin) and/or alcohol; injecting opioid use (especially for novice users with low tolerance).

Signs of intoxication and overdose

Decreased level of consciousness (from drowsiness to coma), slow respiration, bradycardia and miosis ('pinpoint' pupils). Muscle twitching, cyanosis, hypotension, pulmonary oedema and hypothermia may also be present. Death is usually due to respiratory failure, although cardiac arrest may occur secondary to myocardial oxygen deprivation.

Aspiration pneumonia is the most serious condition frequently seen in heroin overdose. Opioids have emetic and cough suppressant properties which, combined with a decreased level of consciousness, can increase the likelihood of aspiration.

Management of intoxication and overdose

Maintenance of airway and breathing are most important in overdose management. Follow cardiopulmonary resuscitation (CPR) protocol.

Administration of naloxone, a short-acting opioid antagonist, will reverse the effect of opioid overdose. Naloxone may be administered by intravenous, intramuscular or subcutaneous injection, or by nasal spray. Patients who were previously sedated may become agitated, aggressive and difficult to manage due to sudden precipitated withdrawal syndrome.

In the case of overdoses involving methadone and long-acting prescribed opioids, naloxone may wear off and the person can become sedated again. Because of the longer half-life of methadone compared with heroin or morphine (methadone = 24-48 hours), people who overdose from methadone and who are subsequently treated with naloxone may seem to recover initially but can relapse into respiratory depression and coma if not adequately monitored and treated. Naloxone infusion may need to be set up for the management of long-acting opioids. High doses of naloxone may be required to reverse the action of certain opioids (e.g. buprenorphine).

Oxygen is generally not advised in the absence of ventilation support as hypoventilation may be masked.

Opioids

Symptoms and onset of withdrawal

The opioid withdrawal syndrome can be very uncomfortable and distressing, but not life-threatening unless there is a severe underlying disease. Patients may have a low tolerance to pain due to the impact of long-term opioid use and this needs to be acknowledged and treated effectively. Onset of withdrawal depends on half-life of individual opioid.

Appearance of withdrawal syndrome in dependent opioid users

Opioid	Time after last dose symptoms appear	Withdrawal syndrome (days)
Heroin/morphine	6-24 hours	5-10 days
Fentanyl (if intravenous)	3-5 hours	4-5 days
Morphine (if intravenous)	8-24 hours	7-10 days
Methadone	36-48 hours	3-6 weeks
Buprenorphine*	3-5 days	Up to several weeks

* except for depot buprenorphine, which is a longer acting formulation prescribed for OAT. See the Clinical guidelines for use of depot buprenorphine: www.health.nsw.gov.au/aod/Pages/brief-depot-bupe-gl.aspx

Symptoms of withdrawal include the following:

Sweating, watery eyes, rhinorrhoea, increased urinary frequency, diarrhoea, nausea, vomiting, abdominal cramps, muscle spasm resulting in headaches, backaches, leg cramps, goose bumps, dilated pupils, elevated blood pressure, tachycardia, anxiety, irritability, dysphoria, sleep disturbance, craving for opioids.

Benzodiazepines and 'Z Drugs'

Overview

Benzodiazepines and the Z-drugs (zolpidem, zopiclone) have sedative-hypnotic effects. They have a general CNS depressant effect that is dose dependent. Benzodiazepines are prescribed for the short-term treatment of stress, insomnia and anxiety disorders and are also used for limited periods in the treatment of AOD withdrawal. Z-drugs are prescribed for the treatment of insomnia.

Pharmacology

Benzodiazepines potentiate the inhibitory effects of gamma aminobutyric acid (GABA) by tightly binding to A-type GABA receptors, resulting in anxiolytic, sedative, hypnotic, muscle relaxant and anti-epileptic effects. Z-drugs act by potentiating the inhibitory effects of GABA through GABA-A receptor positive modulation.

Examples seen in Australia

Absorption rates, half-life, and equivalent daily doses of common benzodiazepines and Z-drugs*

Generic name	Trade name(s)	Time to peak concentration	Elimination half-life	Equivalent dose
Diazepam	Antenax, Valium, Valpam	30-90 min	Biphasic: rapid phase half-life, 3 hours; elimination half-life, 20-48 hours	5 mg
Alprazolam	Alprax, Xanax, Kalma	1 hour	6-25 hours	0.5-1.0 mg
Bromazepam	Lexotan	0.5-4 hours	17 hours	3-6 mg
Clobazam	Frisium	1-4 hours	17-49 hours	10 mg
Clonazepam	Paxam, Rivotril	2-3 hours	31-47 hours	0.5 mg
Flunitrazepam	Hypnodorm	1-2 hours	20-30 hours	1-2 mg
Lorazepam	Ativan	2 hours	12-16 hours	1 mg
Nitazepam	Alodorm, Mogadon	2-3 hours	16-48 hours	2.5-5 mg
Oxazepam	Alrpam, Murelax	2-3 hours	4-15 hours	15-30 mg
Temazepam	Normison, Temaze Temtabs	30-60 min, after tablets, 2 hours after capsules	5-15 hours	10-20 mg
Zolpidem	Stilnox	0.5-3 hours	2.5 hours	Not available
Zopiclone	Imovane, Imrest	1.75 hours	5.26 hours	Not available

* Based on manufacturer's product information.

† Elimination half-life: time for the plasma drug concentration to decrease by 50%.

‡ Equivalent dose: approximate dose equivalent to diazepam 5 mg.

Current usage

There are two main patterns of benzodiazepine dependence, the most common being low-dose dependency over many years, particularly among women and older people. High-dose dependence can also occur, often in the context of polysubstance use. In 2016, 1.6% of Australians were reported to have used benzodiazepines for non-medical purposes in the previous 12 months.

Effects and presentation

Benzodiazepines have anxiolytic, sedative, hypnotic, muscle relaxant and anti-epileptic effects. Z-drugs are generally used only for sedative effects.

Benzodiazepines and 'Z Drugs'

Acute effects (mild intoxication)

Unwanted effects of benzodiazepines include depression, confusion, feelings of isolation or euphoria, impaired thinking and memory loss, headache, drowsiness, sleepiness and fatigue, dry mouth, slurred speech or stuttering, double or blurred vision, impaired coordination, dizziness and tremors, nausea and loss of appetite, and diarrhoea or constipation. Z-drugs may cause diarrhoea, dose-dependent impaired alertness the following morning, and may infrequently cause hallucinations, amnesia, sleepwalking and related behaviour which may be risky. Rarely, paradoxical symptoms of worsened insomnia, irritability and agitation may occur.

Long-term effects

Long-term regular use of benzodiazepines may cause impaired thinking or memory loss, anxiety and depression, irritability, paranoia and aggression, personality change, weakness, lethargy and lack of motivation, drowsiness, sleepiness and fatigue, difficulty sleeping or disturbing dreams, headaches, nausea, skin rashes and weight gain, and addiction.

While it was initially thought that Z-drugs may have less addiction potential than benzodiazepines, dependence, tolerance and misuse comparable to benzodiazepines can occur with long-term use.

Injecting benzodiazepines may also cause vein damage and scarring, infection (including with blood-borne diseases), deep vein thrombosis and clots causing loss of limbs, damage to organs, stroke and possibly death.

Drug interactions

The effects of taking benzodiazepines with other drugs can be unpredictable and dangerous. Benzodiazepines with alcohol or opioids may result in respiratory depression, hypotension, and profound sedation, potentially leading to coma or death.

Using Z-drugs together with alcohol and other psychoactive medicines may increase the likelihood of dangerous behaviour such as sleep walking.

Antipsychotics or other sedating medication including sedating antihistamines can increase the effects of benzodiazepines. A parenteral benzodiazepine given simultaneously with short-acting intramuscular olanzapine is not recommended. Benzodiazepines increase risk of respiratory arrest with clozapine; use with caution and appropriate monitoring, especially at start of treatment.

It has been reported that the use of antidepressant drugs in combination with benzodiazepines may also increase the risk of overdose, especially in the case of older tricyclic antidepressants.

Alcohol and benzodiazepines can produce cross-tolerance, and regular use of both can make withdrawal more severe and/or protracted.

Intoxication and overdose

Benzodiazepines have been identified as causal or contributory in approximately 50% of drug-related deaths, mainly in the context of polysubstance use. Alprazolam appears to be disproportionately associated with misuse and both fatal and non-fatal overdoses and was rescheduled to a Schedule 8 (S8) drug due to concerns about misuse and harms. Flunitrazepam, which has been used as a 'date-rape drug,' is also an S8 drug.

Signs of intoxication and overdose

CNS depression (over-sedation or sleep) is the most common finding after overdose. Respiratory depression may also occur, but is more common following concurrent use with alcohol, opioids and other CNS active drugs. In high doses, patients may manifest coma, respiratory depression, hypotension, bradycardia, hypothermia, and rhabdomyolysis.

Management of intoxication and overdose

As with any overdose, assess the patient's airway, breathing, and circulation, and address rapidly as needed. In any patient with an altered mental status, a blood glucose level should be obtained immediately. The cornerstone of treatment in benzodiazepine overdoses is good supportive care and monitoring. In patients with benzodiazepine overdose complicated by respiratory depression or failure, a concomitant opioid overdose may be present and it is reasonable to administer appropriate doses of parenteral naloxone. Gastrointestinal decontamination with activated charcoal is usually of NO benefit and increases the risk of aspiration.

Flumazenil has little role in the management of benzodiazepine overdose.

Benzodiazepines and 'Z Drugs'

Symptoms and onset of withdrawal

The occurrence of withdrawal syndrome is related to high dosage and long-term use. Short- and intermediate-acting benzodiazepines carry a greater risk of rebound and withdrawal than long-acting benzodiazepines. Alcohol and benzodiazepines can produce cross-tolerance and regular use of both can make withdrawal more severe and/or protracted. Z-drugs are also associated with rebound insomnia, dependence and withdrawal symptoms.

Withdrawal symptoms including anxiety, dysphoria, irritability, insomnia, nightmares, sweating, flu-like symptoms, memory impairment, hallucinations, hypertension, tachycardia, psychosis, tremors, muscle tension and twitching, and seizures may occur after suddenly stopping or reducing the dose too quickly for a dependent person. Onset of symptoms appear within 2-3 half-lives following withdrawal – for short-acting benzodiazepines (e.g. alprazolam) symptoms may occur within 1-2 days; for longer acting benzodiazepines (e.g., diazepam) they may take days or weeks. Symptoms can last for several weeks or longer after prolonged use.

The major complications of withdrawal are progression to severe withdrawal; delirium with risk of injury (to self or others); risk of dehydration or electrolyte imbalance; potential for seizures; presence of concurrent illness, which masks or mimics withdrawal; and orthostatic hypotension.

Psychostimulants

Overview

Psychostimulants include a range of CNS stimulants with sympathomimetic action. They may be prescribed (or potentially used non-medically) or illicit. MDMA is considered a party drug, used at music festivals and dance parties.

Pharmacology

Psychostimulants all act to increase activity of the neurotransmitters dopamine, noradrenaline and serotonin. MDMA and amphetamines act to enhance release of monoamines, whereas cocaine inhibits monoamine re-uptake as well as blocking sodium channel activity.

Examples seen in Australia

Examples of prescribed psychostimulants include methylphenidate (Ritalin[®], Concerta[®]), dexamfetamine and lisdexamfetamine (Vyvanse[®]).

Illicit psychostimulants include amphetamine, methamphetamine, cocaine and MDMA ('ecstasy').

Caffeine is a very commonly consumed stimulant, with milder effects than other stimulants.

Current usage

Use of psychostimulants is widespread nationally, with methamphetamine the most readily available type of amphetamine in Australia. Amphetamines are the second most common principal drug of concern for those presenting for treatment, after alcohol. Use in the 12 months to 2016 reported for MDMA was 2.2%, meth/amphetamine was 1.4% and cocaine was 2.5%. People who regularly use amphetamine-type substances tend to use other drugs in conjunction: in particular, nicotine (tobacco), cannabis and alcohol, and benzodiazepines. Amphetamines may be ingested, injected, smoked or snorted.

Effects and presentation

Stimulants activate the CNS, having a peripheral sympathomimetic action, and are often used for effects such as euphoria, increased sense of wellbeing, increased energy, more confidence or over-confidence, improved cognitive and psychomotor performance, suppression of appetite and reduced sleep.

Acute effects

Loss of appetite, increased heart rate and respiration, nausea and vomiting, dilated pupils, hot and cold flushes, sweating, headaches, pallor, jaw clenching, paranoia, anxiousness, panic attacks, difficulty sleeping, moodiness, irritability and agitation.

Long-term effects

Heart disease, hypertension, stroke, depression, anxiety, insomnia and psychosis, neurocognitive deficits (e.g. memory and attention), weight loss, malnutrition, poor dentition, skin picking.

The use of cocaine or amphetamine derivatives is a strong risk factor for stroke or other forms of acute cerebrovascular emergencies including haemorrhagic or thromboembolic strokes and cerebral haemorrhage.

Drug interactions

Combining psychostimulants with nonselective monoamine oxidase inhibitor (MAOI) is likely to result in a hypertensive crisis and possibly cause intracranial haemorrhage or acute heart failure; avoid combination (contraindicated by manufacturer). Taking a psychostimulant with moclobemide (a reversible inhibitor of MAOA) may also result in hypertensive crisis.

Combining two or more sympathomimetic agents may increase the risk of related adverse effects, especially on the cardiovascular system (e.g. increased blood pressure, tachycardia). Monitor patients for additive sympathomimetic effects including hypertension, acute myocardial infarction and ventricular arrhythmias.

High doses of caffeine in energy drinks can increase risks of toxicity when consumed with alcohol or other stimulants.

Psychostimulants

Amphetamines may enhance the adverse/toxic effect of serotonin modulators. The risk of serotonin syndrome may be increased. Monitor patients closely for signs and symptoms of serotonin syndrome if amphetamines and serotonin modulators are used in combination. MDMA is the most serotonergic drug in this group, thus may pose a greater risk than other agents. This risk is further enhanced if MDMA or other amphetamine derivatives are used in combination with drugs that contribute to serotonin toxicity (e.g. antidepressants, certain opioids, lithium). The clinical features include clonus, agitation, diaphoresis, tremor, tachycardia, hyperreflexia, hypertonia and hyperthermia.

Cannabinoid-containing products may enhance the tachycardic effect of sympathomimetics. Monitor cardiovascular status closely if cannabinoids and sympathomimetics are combined.

Intoxication and overdose

In adults, the acute lethal dose of amphetamine has been reported to be 20 to 25 mg/kg. Patients who chronically use amphetamines develop tolerance, and up to 15,000 mg/day has been ingested without lethal result.

Signs of intoxication and overdose

Signs of amphetamine overdose include tachycardia, hypertension, hyperthermia, diaphoresis and mydriasis. Alterations in mental status can include anxiety, agitation, violent behaviour and seizures. Secondary complications can involve the kidneys, skeletal muscles and gastrointestinal system. The most common causes of death related to amphetamine toxicity are arrhythmia, hyperthermia and intracerebral haemorrhage. Severe MDMA overdoses are associated with intense sympathomimetic responses and active hallucinations as well as thermoregulatory, neurologic, cardiovascular, hepatic and electrolyte disturbances. Neurological symptoms include agitation, hallucinations, seizures, coma and acute and chronic psychiatric symptoms.

Rhabdomyolysis is a serious potential consequence of methamphetamine, cocaine and MDMA toxicity. Symptoms include muscle pain, weakness, and dark urine. Additional symptoms that are more common in severely affected patients include malaise, fever, tachycardia, nausea and vomiting, and abdominal pain.

Management of intoxication and overdose

Uncomplicated intoxication may only require observation and monitoring for several hours in a subdued environment until symptoms subside. Management is predominantly supportive, with an emphasis on sedation and reduction of body temperature. Some patients also require pharmacologic therapy for control of hypertension.

Use of amphetamines may cause thirst. Large consumption of water may lower the blood concentration of electrolytes. Monitoring of blood results for electrolytes and kidney function is advisable. Patients who complain of chest/muscle pain should have creatinine kinase (CK), troponin and chest X-ray investigations. An electrocardiogram (ECG) is needed.

Symptoms and onset of withdrawal

Withdrawal is characterised by three phases: crash, withdrawal and extinction.

Crash occurs within 12–24 hours of last use of amphetamine (a few hours with cocaine) and lasts for 2–4 days (1–2 days with cocaine). Symptoms include low cravings, sleep disturbances, mood disturbances—typically flat mood or dysphoria and may be associated with anxiety or agitation, exhaustion, fatigue, generalised aches and pains.

Withdrawal typically commences 2–4 days after last amphetamine use, peaking in severity over 7–10 days, and subsides over 2–4 weeks. Cocaine withdrawal typically commences 1–2 days after last use, peaking in severity over 4–7 days, and subsides over 1–2 weeks. Symptoms include strong cravings, fluctuating mood and energy levels, alternating between irritability, restlessness, anxiety, and agitation. Fatigue, lacking energy, anhedonia. Disturbed sleep, including vivid dreams, insomnia. General aches and pains, headaches, muscle tension, increased appetite, poor concentration and attention. Disturbances of thought (e.g. paranoid ideation, strange beliefs) and perception (misperceptions, hallucinations) can re-emerge during withdrawal phase after having been masked during crash.

Extinction occurs weeks to month after last use. Symptoms include gradual resumption of normal mood with episodic fluctuations in mood and energy levels, alternating between irritability, restlessness, anxiety, agitation, fatigue, lacking energy and anhedonia. Episodic cravings and disturbed sleep.

Cannabis

Overview

Cannabinoid is the generic name given to the psychoactive substances found in the marijuana plant *Cannabis sativa*. It is a commonly used psychoactive substance worldwide. The main active cannabinoid is delta 9-tetrahydrocannabinol (THC). The other main cannabinoid is cannabidiol (CBD) which is thought to have an anti-psychoactive effect and may moderate the 'high'.

Cannabis can be smoked alone or with tobacco, within a regular or water pipe or rolled in paper, or ingested, typically in food.

Cannabis products (e.g. nabiximols) have been used medicinally for spasticity due to multiple sclerosis. Nabiximols contain THC and CBD in approximately equal amounts.

Pharmacology

Cannabis is a CNS depressant, but also alters sensory perceptions and may produce hallucinogenic effects when large quantities are used.

THC acts on cannabinoid receptors CB1 and CB2:

- CB1 is found in the CNS and inhibits release of neurotransmitters including acetylcholine, L-glutamate, GABA, noradrenaline, dopamine and 5-HT
- CB2 is found peripherally in the immune system tissues, peripheral nerve terminals and vas deferens. It is postulated that it plays a role in regulation of immune responses and inflammatory reactions.

Examples seen in Australia

Cannabis comes in three main forms:

- Herbal cannabis – the dried leaves and flowers of the cannabis plant (the weakest form)
- Cannabis resin (**hashish**) – the dried resin from the cannabis plant
- Cannabis oil (**hashish oil**, '**dabs**') – the oil extracted from the resin (the strongest form).

Cannabis is also referred to as **marijuana**.

Synthetic cannabis (e.g. '**kronic**') is a drug of concern originally designed to mimic psychoactive effects of cannabis.

Current usage

Cannabis is the most widely used illicit drug in Australia and usage has remained stable, increasing from 29% in 2001 to 34% in 2016, with 10.4% of people using cannabis in the preceding 12 months.

Use of synthetic cannabis in the 12 months to 2016 is reported to have declined to 0.3% from 1.2% in 2013.

Effects and presentation

Cannabis affects every individual differently – even the same person may have a different experience on separate occasions, depending on size, weight and health, previous use, other drugs being taken, amount and strength of drug, individual expectations, environment and personality.

Acute effects (mild intoxication)

The effects of cannabis may be felt immediately if smoked, or within an hour or two if eaten, and may include feelings of relaxation and euphoria, spontaneous laughter and excitement, increased sociability, elevated heart rate, increased appetite, dry mouth, impaired memory, loss of coordination, bloodshot eyes, dryness of the eyes, mouth and throat, anxiety and paranoia. Sedation may occur at higher doses.

Synthetic cannabis can cause adverse effects including acute kidney injury, seizures, stroke and death.

Long-term effects

Long-term effects are dependent on how much and how often the cannabis is consumed and how the cannabis is consumed. Heavy, regular use of cannabis may eventually cause tolerance to the effects of cannabis; dependence on cannabis; reduced cognitive functioning and decreased motivation in areas such as work or concentration. There is growing concern regarding the increased risk of developing psychosis with cannabis use.

Smoking cannabis may increase the risks of sore throat, asthma, bronchitis, and, if smoked with tobacco, cancer.

A small number of people who use cannabis long-term, may develop Cannabinoid hyperemesis syndrome which causes repeated and severe vomiting and nausea, which resolves with discontinuation of use.

Drug interactions

Combining cannabis with alcohol can cause nausea and vomiting. Some people use cannabis to help with the 'come down' effect of stimulant drugs; this may mask the symptoms of the latter and end up in overdose.

Intoxication and overdose

Recreational cannabis intake to achieve psychoactive effects can often result in adverse effects because there is no clear indication of doses that achieve symptoms desired by a marijuana user vs noxious effects. The effects of cannabis also vary between people and may even be different for the same person at different times.

Signs of intoxication and overdose

Signs of cannabis intoxication in adolescents and adults include tachycardia; increased blood pressure or, especially in older people, orthostatic hypotension; increased respiratory rate; conjunctival injection (red eye); dry mouth; increased appetite; nystagmus; ataxia; and slurred speech.

Complications associated with inhalation of cannabis include acute exacerbations and poor symptom control in patients with asthma; pneumomediastinum and pneumothorax suggested by tachypnoea, chest pain, and subcutaneous emphysemas caused by deep inhalation with breath holding; and rarely, angina and myocardial infarction.

Management of intoxication and overdose

The management of cannabis intoxication consists of supportive care and symptom management.

Mild intoxication with dysphoria is common in either naive or chronic cannabis users after using a high-potency product. Most patients can be managed with a dimly lit room, reassurance and decreased stimulation. Short-term use of benzodiazepines may help with anxiety.

Severe physiological effects, marked agitation and combativeness not responsive to reassurance and benzodiazepines is rare after cannabis use and should prompt the clinician to consider combined use with other recreational drugs including cocaine, amphetamines and phencyclidine, or coexisting mental illness.

Symptoms and onset of withdrawal

Withdrawal from cannabis, unlike withdrawal from synthetic cannabinoids, is not generally associated with clinically significant cardiovascular changes or symptoms such as sympathetic autonomic hyperactivity.

Most cannabis withdrawal symptoms appear 24–72 hours after cessation of use, reach peak intensity over the first week, and largely resolve after 1–2 weeks. Sleep disturbances may last several weeks.

Symptoms of mild withdrawal may include mild sleep disturbance and anxiety but performing normally at work/school.

Moderate to severe withdrawal affects daily functioning and/or likelihood of relapse and may benefit from treatment. Symptoms include severe sleep disturbance resulting in excessive daytime drowsiness that interferes with work or school; irritability, anger, anxiety, depression and restlessness; decreased appetite or weight loss; abdominal pain; shakiness or tremors; sweating, fever or chills; and headache.

Cannabis is considered psychotogenic and, in vulnerable individuals, can exacerbate or trigger psychosis during intoxication and occasionally in cannabis withdrawal states. If signs of psychosis are observed during withdrawal, refer to emergency department and appropriate mental health services post-withdrawal.

Nicotine

Overview

Nicotine is the major psychoactive substance in tobacco and has both stimulant and relaxing effects. Considerable tolerance to and dependence on nicotine develop over time.

Pharmacology

Nicotine binds to nicotinic cholinergic receptors, mediating the complex actions of nicotine in tobacco users. Dopamine, glutamate and GABA release are particularly important in the development of nicotine dependence.

Examples seen in Australia

Nicotine in tobacco is usually smoked in cigarettes. It is also smoked in cigars and pipes. Cigarettes account for around 98% of tobacco consumed in Australia. E-cigarettes may also contain nicotine and a range of chemicals such as solvents and flavouring agents. Use of e-cigarettes is also known as 'vaping'.

Other forms of consumption include loose tobacco ('chop-chop') and waterpipe smoking. Some batches of chop-chop contain fungal (mould) spores which can cause a range of health problems if inhaled.

Current usage

The daily smoking rate in Australia did not significantly decline over the most recent 3-year period (12.8% in 2013 and 12.2% in 2016). However, the long-term downward trend has been a steady reduction over the last two decades and has halved since 1991 (24%).

In 2017, among students aged 16-17, 21% had tried e-cigarettes.

Effects and presentation

Inhaling smoke from cigarettes is an extremely efficient method for delivering nicotine, which dissolves instantly in saliva lining in the mouth and travels into the bloodstream in a few seconds. The smoker may experience immediate effects of dizziness and feeling light-headed.

Acute effects

Initial stimulation, then reduction in brain and nervous system activity; mild euphoria; enhanced alertness and concentration; feelings of relaxation; increased heart rate; nausea, acid in the stomach, reduced appetite, stomach cramps and vomiting; watery eyes; mild stimulation; coughing; dizziness; headaches; bad breath; tingling and numbness in fingers and toes, reduced appetite, stomach cramps and vomiting.

Long-term effects

Cancer of the lung, throat, mouth, lips, gums, kidney and bladder, heart disease and stroke, emphysema and other lung diseases, gangrene and other circulatory diseases, blindness from macular degeneration and cataracts, osteoporosis, impotence, infertility and miscarriages.

Drug interactions

Nicotine used with benzodiazepines can reduce the effectiveness of benzodiazepines, possibly due to the CNS stimulation from nicotine. If patients try to quit smoking while on benzodiazepines, this may result in CNS depression.

Smoking increases the risk of thromboembolism, ischaemic stroke and myocardial infarction in women taking the combined oral contraceptive pill. Combined oral contraceptive pills are contraindicated in women over 35 years old who smoke 15 cigarettes or more a day.

Interactions can result from tobacco smoke inducing cytochrome P450 (CYP1A2 and CYP2B6) enzymes in the liver, affecting the metabolism of caffeine, alcohol and certain medications, such as certain antidepressants (e.g. fluvoxamine and imipramine), antipsychotics (e.g. clozapine and olanzapine) anticoagulants (e.g. warfarin and heparin) and methadone.

Methadone has been shown to increase satisfaction from smoking and may also reduce the withdrawal effects of nicotine. If a patient is trying to quit smoking, it is recommended that specialist support is sought if trying to reduce methadone dose.

Interactions are caused by components of tobacco smoke—not nicotine—and nicotine replacement therapy will not affect changes in medication levels caused by smoking cessation. Upon cessation of smoking, doses of medication may need to be adjusted.

Nicotine

Intoxication and overdose

When nicotine is consumed in excessive amounts, it can lead to respiratory failure and cardiac arrest.

Signs of intoxication and overdose

If a large amount of nicotine is taken, it may cause confusion, feeling faint, seizures, respiratory arrest, bradycardia, hypotension and death. Overdosing on NRT is rare.

Management of intoxication and overdose

Monitoring and supportive care are indicated. Atropine and benzodiazepines may be used as part of supportive care.

Symptoms and onset of withdrawal

People experience nicotine withdrawal differently. Most people experience some of the symptoms of nicotine withdrawal and they usually don't all happen at once. Some people are successful at quitting unaided. For most people, assistance is required to encourage and support attempts to quit, manage symptoms of nicotine withdrawal and prevent relapse.

Withdrawal symptoms usually start within 2–3 hours after last use and may last from a few days to a few weeks. Symptoms include cravings, irritability, anxiety and depression, restless sleep, eating more and putting on weight, trouble concentrating, headaches, coughing and sore throat, aches and pains, upset stomach and bowels.

It is common practice to under-dose on Nicotine Replacement Therapy (NRT), resulting in ongoing withdrawal symptoms. It is always safer to use multi-patching and/or extra oral NRT products to manage withdrawal symptoms, than to resort to smoking.

Hallucinogens

Overview

Hallucinogens produce distortions in thoughts, mood and perceptions – typically inducing illusions or hallucinations. They are most commonly used in one-off social contexts such as dance or rave parties, clubs and pubs, or at home.

Pharmacology

It is believed that hallucinogens alter sensory perceptions by stimulating 5-HT_{2A} receptors, especially those expressed on neocortical pyramidal cells. Psychedelic effects of typical recreational doses of LSD last 6 to 12 hours.

Examples seen in Australia

Lysergic acid diethylamide (**LSD**), phencyclidine (**PCP, Angel dust**), psilocybin (**magic mushrooms**), and dimethyl tryptamine (**DMT**). Note: MDMA (methylene dioxy-amphetamine) (ecstasy) is a psychostimulant that also has hallucinogenic properties. **NBOMes** are a synthetic substance designed to mimic the effects of LSD and belong to a group called Novel Psychoactive Substances (NPS).

Current usage

The reported use of hallucinogens in the 12 months leading to 2016 declined slightly compared to 2013 from 1.3% to 1.0%. This decline was driven by reported changes in use by males.

Effects and presentation

The effects differ among individual users and are determined by the amount (and strength) of the preparation, the size, weight and health of the person, whether they are used to taking it, and whether other drugs have been taken. Users may occasionally experience a 'bad trip' and suffer from disturbing hallucinations.

Acute effects (mild intoxication)

Euphoria and wellbeing, dilation of pupils, seeing and hearing things that aren't there (hallucinations), confusion and trouble concentrating, depersonalisation, derealisation, headaches, nausea, fast or irregular heartbeat, increased body temperature, breathing quickly, vomiting, facial flushes, sweating and chills.

Long-term effects

Flashbacks (similar to the drug effect, sometime after last use) may persist for months or years after use depending on the magnitude and usage over time. Flashbacks can be precipitated by other drugs (e.g. cannabis), anxiety and fatigue – and are most commonly associated with LSD and PCP.

Psychiatric disturbances such as prolonged psychosis, depression, personality disruption and post-hallucinogen perceptual disorder have been attributed to prolonged use. Hallucinogens are not thought to induce psychotic disorders but may unmask latent psychiatric illness.

Other long-term effects include decreased memory and anxiety.

Drug interactions

The effects of taking hallucinogens with other drugs can be unpredictable and dangerous (e.g. using LSD with ice, speed or ecstasy can increase the chances of a bad trip and can also lead to panic; using LSD with alcohol increases incidences of nausea and vomiting).

Intoxication and overdose

Many patients intoxicated with hallucinogens are awake, aware that their symptoms are drug-induced, and able to provide a history of recreational hallucinogen use. Seizure and rhabdomyolysis have been reported in extreme cases. Severe injury or death (e.g. from drowning) more commonly occur as a result of impaired judgment and warped sense of distance, time and reality while intoxicated.

Hallucinogens

Signs of intoxication and overdose

Unwanted neuropsychiatric effects include fear, panic reactions, dysphoria, frightening imagery and an overwhelming sense of dread.

Symptoms of PCP intoxication include bizarre or violent behaviour, nystagmus (vertical and horizontal) and incoordination. Disorientation, severe agitation, violent behaviour, auditory hallucinations and catatonic stupor occur at higher doses. Hypertension and tachycardia are often seen but generally do not require specific therapy.

Hyperthermia seldom occurs with isolated hallucinogen intoxication but denotes severe toxicity that requires aggressive management in a critical care setting. When hyperthermia does occur, psychomotor agitation is the most common cause.

Due to its high and variable potency, NBOME toxicity has been associated with deaths in recent years due to intoxication and behaviour resulting from severe symptoms.

Management of intoxication and overdose

In most cases, supportive care is enough to manage patients acutely intoxicated with hallucinogens. Patients should be placed in a calm, quiet environment until symptoms of intoxication abate. These symptoms are self-limited and not usually severe; a conservative approach is preferred unless there is evidence of severe toxicity (e.g. hyperthermia and severe agitation).

Benzodiazepines are first-line therapy for acute agitation and dysphoria. If psychotic symptoms persist (e.g. after agitation subsides), neuroleptics such as haloperidol may be titrated with careful monitoring.

Confusion, overt psychosis, severe agitation, or markedly abnormal vital signs should prompt a search for alternative diagnoses.

Differentiation may be possible based upon the character of the hallucinations: stimulant-induced hallucinations are usually auditory, whereas hallucinogen-induced hallucinations are usually visual. Also, stimulants tend to be associated with more severe tachycardia and hypertension.

Medical causes of altered mental status that should be ruled out immediately include hypoglycaemia, hypoxia and head trauma. Other considerations include withdrawal from ethanol or sedative-hypnotics, infection of the central nervous system/urinary tract, serotonin syndrome and neuroleptic malignant syndrome (NMS), and primary psychiatric disorders.

Anticholinergic delirium produces tachycardia, mydriasis and altered mental status, but affected patients are usually confused with garbled speech. Patients intoxicated with the common hallucinogens described above tend to be oriented and speak clearly.

Symptoms and onset of withdrawal

Hallucinogens do not appear to result in significant physical dependence but there have been reports of psychological dependence occurring.

People withdrawing from LSD may experience cravings, fatigue, irritability and reduced ability to experience pleasure.

Inhalants and solvents

Overview

Inhalants and solvents are sometimes referred to as volatile substances. They include a wide variety of easily obtained products and substances that can be misused by either sniffing or inhaling the vapours ('chroming').

Pharmacology

Inhalants act as CNS depressants. CNS depression is thought to be mediated by alteration of neuronal membrane function at glutamate or GABBA receptors.

Examples seen in Australia

Inhalants are usually common household and industrial products such as glue, paint, dry cleaning fluids, petrol, cigarette lighter gas, propellants from whipped cream, correction fluids, nitrous oxide and amyl nitrite. The product is inhaled through the nose or mouth. It is often sprayed into a paper/plastic bag or soaked onto a cloth or sleeve and then inhaled. It can also be inhaled directly from the container or a cool drink bottle.

Current usage

The use of inhalants has increased over the last 15 years, increasing from 0.4% to 1% of Australians using inhalants in the 12 months preceding 2016.

Effects and presentation

The effects of inhalants may start to be felt immediately and can last from 2–3 minutes up to 45 minutes.

Acute effects (mild intoxication)

Euphoria, feeling of 'high', giggling and laughing, hallucinations, drowsiness, headaches, bloodshot or glazed eyes, blurred vision, nosebleeds, rhinorrhoea, sneezing, unpleasant breath, slurred speech, chest pain, ataxia, low blood pressure, arrhythmia, nausea, vomiting and diarrhoea.

Long-term effects

Irritability and depression; memory loss; neurocognitive impairment; tremors; weight loss; tiredness; problems with blood production, which may result in anaemia, irregular heartbeat, heart muscle damage, chest pain and angina; indigestion and stomach ulcers; liver and kidney damage; pimples; rashes or blisters around the mouth and lips; tolerance and dependence.

Most of these long-term effects can be reversed if use is stopped. However, some inhalants, such as cleaning products, correction fluid, aerosol sprays and petrol can cause permanent damage. Prolonged use of nitrous oxides may result in vitamin B12 (cobalamin) depletion, memory loss, muscle weakness/numbness, incontinence, limb spasms and psychosis.

Drug interactions

Combining inhalants with other depressant drugs such as alcohol, benzodiazepines or opioids can affect the respiratory and cardiovascular system, increasing the risk of overdose. Mixing drugs can also increase the risk of passing out and suffocating or choking on vomit.

Intoxication and overdose

Risks of overdose and adverse outcomes is increased if sniffing in enclosed spaces, when running or doing other physical activity after sniffing (which can cause death due to cardiac sensitisation), mixing sniffing with medicines or illegal drugs, or sniffing while affected by health problems. Sudden sniffing death is a rare outcome after chroming due to cardiovascular collapse; it is unpredictable and can happen to first-time users. Respiratory depression and seizures may also happen.

Rarely, the use of benzene derivatives, nitrates and nitrites may cause acquired methemoglobinemia – symptoms result from an acute impairment in oxygen delivery to tissues and include cyanosis with pale, grey or blue coloured skin, lips and nail beds, light-headedness, headache, tachycardia, fatigue, dyspnoea, and lethargy. Acquired methemoglobinemia may become symptomatic when methemoglobin comprises more than 10% of total haemoglobin. At higher methemoglobin levels, respiratory depression, altered sensorium, coma, shock, seizures and death may occur. Clinicians should be aware that pulse oximetry is not a reliable measurement of the severity of methemoglobinemia; oxygen saturation rarely drops below 85% despite severe methemoglobinemia. Treatment options include high-dose oxygen and intravenous methylene blue.

Inhalants and solvents

Signs of intoxication and overdose

Symptoms include nausea, vomiting and diarrhoea, irregular heartbeat, chest pain, hallucinations, blackout, seizures and coma.

Inhaling aerosol sprays has been known to cause sudden death. It is believed that chemicals in these products can cause heart failure, particularly if the person is stressed or does heavy exercise after inhaling. This is very rare, but warrants hospital monitoring even for first-time users.

Management of intoxication and overdose

Approach in a very calm manner, as sudden movements (e.g. running) by the solvent-affected person can cause severe cardiac arrhythmia. Remove the inhalant and make sure the person gets plenty of fresh air. Management of acute inhalant intoxication is supportive, prioritising maintenance of cardiorespiratory function.

Symptoms and onset of withdrawal

Withdrawal syndrome can occur in some cases of solvent abuse – symptoms are usually mild. Amyl nitrites and nitrous oxides rarely lead to physical withdrawal symptoms, apart from craving to use more.

Onset may occur 24–48 hours after the last use and may last 2–5 days. Symptoms can include anxiety, depression; dizziness; drowsiness, tiredness; headache; nausea and stomach pain; shakiness, tremors and muscular cramps; hallucinations and visual disorders, such as seeing spots; and in severe cases, seizures may occur.

Ketamine

Overview

Ketamine hydrochloride, a derivative of phencyclidine (PCP), is a dissociative anaesthetic that has stimulant properties when taken in low doses. The effects appear subjective depending on individual characteristics of the patient and the setting in which it is used.

Pharmacology

Ketamine is a drug with multiple mechanisms of action including antagonism of N-methyl-D-aspartate (NMDA) receptors and interaction with muscarinic receptors, descending monoaminergic pain pathways, voltage-sensitive calcium channels and opioid receptors in the brain and spinal cord. The degree to which each contributes to the different effects experienced through using ketamine is not clear.

Examples seen in Australia

Ketamine is an anaesthetic registered in Australia for use for induction and maintenance of anaesthesia, as a sole anaesthetic or as an adjunct to other agents. Small trials investigating the use of ketamine for treatment-resistant depression are also being conducted.

Current usage

1.9% of Australians have used ketamine one or more times in their life with 0.4% of people reporting use in the 12 months to 2016. When sold illegally, ketamine usually comes as a white crystalline powder and is commonly snorted. It can also be made into tablets and pills or dissolved in a liquid. It can be swallowed or injected.

Effects and presentation

Ketamine produces a feeling of detachment from one's body and the external world. It does this by reducing or blocking signals to the conscious mind from other parts of the brain, typically the senses. It also has hallucinogenic effects and can impact on the senses and perception of reality. Ketamine users can experience an 'emergent state' also called a 'K-hole', which is a trip-like experience that varies from person to person.

Seizures may occur in people with known seizure disorders (literature reports that ketamine may induce or terminate seizures). Psychotic symptoms can be triggered in some people (e.g. those with schizophrenia).

Acute effects (mild intoxication)

Short-term effects at low doses can produce a state resembling alcohol intoxication, with ataxia, euphoria, slurred speech, nystagmus, numbness of the extremities, and cardiovascular and respiratory stimulation. Other short-term effects include increased libido, a sense of floating, drowsiness, amnesia, nausea and vomiting.

Long-term effects

Flashbacks; poor sense of smell (from snorting); mood and personality changes including depression; poor memory, thinking and concentration; abnormal liver or kidney function; ketamine bladder syndrome (symptoms include difficulty holding in urine and incontinence, which can cause ulceration in the bladder); abdominal pain ('K-cramps'); tolerance and dependence.

Drug interactions

Concurrent use of sympathomimetics including amphetamines, MDMA and cocaine may lead to increased sympathomimetic effects of ketamine, putting greater strain on the cardiovascular system.

The use of ketamine with other CNS depressants (e.g. alcohol and opioids) can potentiate CNS depression and/or increase risk of developing respiratory depression.

Benzodiazepines may increase the half-life of ketamine and prolong its pharmacodynamic effects.

Intoxication and overdose

Risks of overdose are increased when combined with other drugs such as depressant drugs (including alcohol) and tranquillisers (including benzodiazepines and opioids).

At higher doses, the predominant acute effects include sweating, drowsiness, hypersalivation, fever, myoclonus, blurred vision, apathy, dissociative 'out of body' sensations, muscle rigidity, reduced response to pain, risk of respiratory collapse or failure, feelings of aggression, hostile and bizarre behaviour, stimulation, disorganised thoughts, temporary paralysis, hallucinations, euphoria, seizures, confusion, disorientation and coma.

Signs of intoxication and overdose

Inability to move, rigid muscles, high blood pressure, fast heartbeat, convulsions, unconsciousness and 'near death' experiences, death (which is rare, unless combined with other drugs).

Management of intoxication and overdose

Once airway, breathing and circulation are secured, supportive care is usually the only treatment necessary for ketamine toxicity. The adverse effects of ketamine last between 15 minutes to several hours, and prolonged care is rarely needed. Psychiatric disturbance from ketamine toxicity is generally short-lived. Minimise stimuli such as light and noise. Benzodiazepines may be indicated if chemical sedation is required (e.g. to manage fear, panic, hallucinations, and emergence reactions). Lorazepam may be used in 1-2 mg intravenous doses, until the desired level of sedation is achieved. Alternatively, diazepam in 5-10 mg intravenous doses may be used.

Symptoms and onset of withdrawal

Withdrawal symptoms usually last for 4-6 days.

Symptoms include cravings for ketamine, no appetite, tiredness, chills, sweating, restlessness, tremors, nightmares, anxiety, depression and irregular and rapid heartbeat.

Gamma hydroxybutyrate (GHB)

Overview

GHB is a CNS depressant with similar action to benzodiazepines. Its effects are highly dose-dependent.

Pharmacology

GHB is an agonist for the GHB and GABA_B receptors. It has a half-life of approximately 30 minutes.

Examples seen in Australia

GHB usually comes as a colourless, odourless, bitter or salty liquid, which is usually sold in small bottles or vials. It can also come as a bright blue liquid known as 'blue nitro', and less commonly as a crystal powder. It is also known as '**G**' and '**fantasy**'.

Current usage

The rate of GHB use in Australia has not changed much over the last 15 years – 0.1% had used GHB in the 12 months to 2016. GHB is usually swallowed, but sometimes it's injected or inserted anally.

Effects and presentation

GHB has a rapid onset of action (<15 minutes) with peak effects after 60 minutes and a total duration of action of 2–4 hours.

Acute effects (mild intoxication)

Feelings of euphoria, increased sex drive, relaxation and tranquillity, drowsiness, decreased inhibition, increased confidence, enhanced sense of touch, nausea, diarrhoea, blurred vision, tremors, sweating and hot and cold flushes.

Long-term effects

There is limited information about the long-term effects of GHB, but regular use can lead to tolerance and dependence.

Drug interactions

Use of GHB with alcohol and benzodiazepines can increase the risk of overdose. Mixing alcohol with GHB can at first reduce the effects of GHB, which can lead some to take a higher dose.

Combining GHB with amphetamines or MDMA puts enormous strain on the body and increases risk of seizures.

Intoxication and overdose

The chemical composition of GHB is highly variable and this can increase the risk of overdose (a small increase in amount can result in a dramatic increase in effect). Alcohol is particularly dangerous in combination with GHB as it can be difficult to control the dose. Overdose is a significant risk in such situations.

Signs of intoxication and overdose

Decreased level of consciousness, coma and seizures; impaired movement and speech; severe respiratory depression; hypothermia; respiratory acidosis; vomiting; hypotension; bradycardia; agitation and delirium upon waking up.

Management of intoxication and overdose

Treatment of intoxication is essentially supportive and requires monitoring vital signs and ensuring the airways are clear. Cardiovascular symptoms don't normally require therapy; hypotension alone may be managed by intravenous fluids; atropine may be administered to treat bradycardia if there is associated hypotension.

Aspiration may result from emesis if the patient is unconscious – consider intubation during the first few hours of recovery if the patient is unconscious.

Symptoms and onset of withdrawal

The signs and symptoms of GHB withdrawal vary from patient to patient depending on extent and duration of prior drug exposure.

The first symptoms of GHB withdrawal tend to appear 12–24 hours after the last exposure, when people start to become nervous and anxious and have difficulty sleeping. Withdrawal from GHB may last two weeks or longer. Symptoms can include confusion or delirium, agitation, anxiety, panic, insomnia, shaking, muscle cramps, perspiration, hallucinations, tachycardia, seizures/convulsions, delusions or paranoia, psychosis, sweats, hypertension, nausea or vomiting, blackouts, and bowel and bladder incontinence.

Anabolic androgenic steroids (AAS)

Overview

Anabolic steroids are classed as performance and image-enhancing drugs. They are synthetic hormones that imitate male sex hormones, specifically testosterone.

They may be prescribed medically for male hypogonadism, to improve bone density, and to increase body weight and muscle mass in wasting syndromes associated with HIV.

Pharmacology

AAS bind to and activate androgen receptors that regulate androgen-responsive genes involved in the development and maintenance of masculine sexual characteristics. Androgens also have systemic anabolic and psychological effects.

Examples seen in Australia

There are many different brand names of anabolic steroids, developed for either human or veterinarian use, which differ slightly in chemical structure. Typically, steroids are either taken orally in tablet form or via intramuscular injection, but there are also some gels or creams that are applied to the skin.

Current usage

Use of AAS has remained stable over many years. The 2016 National Drug Strategy Household Survey found that 0.6% of the population reported any lifetime use of steroids for non-medical purposes, and 0.1% had used steroids in the past year, but this may be an underestimate.

Effects and presentation

Generally, people who use AAS experience an increase in muscle strength very quickly. This means that people are able to train more often and for longer periods of time, with improved recovery.

Acute effects

AAS use can lead to a rapid increase in lean muscle tissue, but fluid retention is common and causes muscles to look soft or bloated. AAS affect everyone differently. Experiences can include increased strength; increased confidence and sense of wellbeing; acne – leading to permanent scarring; irritability and mood swings; more frequent colds; aggression and violence; increased sex drive; and sleeping difficulties.

Long-term effects

Liver damage, kidney or prostate cancer, high blood pressure, depression, cardiovascular complications, tendon/ligament damage.

Men: reduced sperm count and fertility, shrunken testicles, baldness, gynaecomastia (developing breasts), involuntarily and long-lasting erection.

Women: facial hair growth, irregular periods, deepened voice, smaller breasts and enlarged clitoris.

Injecting steroids increases the likelihood of contracting bacterial infections and skin abscesses and can cause permanent nerve damage, which can lead to sciatica. Injecting in unhygienic environments or sharing equipment with others also increases the risk of contracting blood-borne viruses.

Drug interactions

The risks of taking higher doses and combining steroids with other performance and image-enhancing drugs or other medications are not fully understood. Combining one steroid with another (stacking) or with an illicit drug (e.g. cocaine) or masking agent (e.g. diuretics) may result in serious adverse effects including heart attack, stroke and death.

Stimulants and cocaine: when combined with stimulants there may be increased heart rate, increased blood pressure and depression. Cocaine is shorter-acting, and can also cause increased body temperature, myocardial infarction and CVA, euphoria, masked pain, feelings of aggressiveness and competitiveness, and increased libido. Psychological depression may occur when ceasing combined use of cocaine and steroids.

Diuretics: used with steroids can alter the sodium/potassium balance in the body. This may cause exhaustion, kidney damage, muscle weakness, cardiac arrest and death.

Anabolic androgenic steroids (AAS)

Overdose

Particularly when high doses are used outside medical guidance, AAS may cause irreversible heart damage if used in high doses for prolonged periods. Steroid use has also been associated with liver damage.

Signs of intoxication and overdose

AAS are not usually associated with acute overdose when used alone, but rather an accumulation of negative effects over long-term use.

Acute intoxication and overdose are more likely to occur when anabolic steroids are used with a stimulant (e.g. cocaine, MDMA, amphetamine). Signs include heart attack, stroke and death.

Management of intoxication and overdose

Supportive care is recommended, monitor vital organs.

Symptoms and onset of withdrawal

Regular steroid users may experience a need or craving if they stop taking the drug.

Anabolic steroids do not cause physical dependence, but people can find themselves relying on them to build confidence and self-esteem. This reliance can make it difficult to stop using them in the longer term. Prolonged steroid use can result in the suppression of natural testosterone production for a period of time, resulting in physical withdrawal symptoms such as changes in sex drive and sleep.

Symptoms experienced after completing an anabolic steroid cycle include extreme tiredness, weight loss due to decreased appetite, decreased strength, nervousness, irritability and depression.

Emerging drugs of concern

Fentanyl, fentanyl analogues and carfentanil – refer to Opioids

Fentanyl is available in several forms including lozenges and injection. In Australia, the most common form of fentanyl prescribed is a patch, which is applied to the skin. Though the use of fentanyl is relatively small compared to heroin, it increased 10-fold from 2012 to 2015. Fentanyl is one of the opioids that may contribute to serotonin toxicity.

Fentanyl is 50–100 times more potent than morphine and some even stronger analogues (e.g. carfentanil) are entering the drug supply as counterfeit tablets, liquid or substituted for heroin. International reports suggest increased market presence of fentanyl and its analogues mixed with stimulants such as methamphetamine. The high potency makes it difficult for people to know how much they are using.

In Australia between 2000 and 2011, 136 fentanyl-related deaths were recorded:

- 54% had a history of injecting drug use and 95% had injected fentanyl at the time of death
- deaths were primarily among Australians aged under 47 years.

Carfentanil is up to 100 times more potent than fentanyl, and exposure routes include topical, inhalation, ingestion and needle-stick. Healthcare workers are advised to use protective equipment when handling substances.

Recently in NSW, acetyl-fentanyl and fentanyl overdoses have been confirmed in people who believed they were using cocaine or methamphetamine (but were sold acetyl-fentanyl or fentanyl).

Pregabalin and gabapentin

Overview

Pregabalin and gabapentin are gabapentinoids, a class of anti-epileptic agents that are also prescribed for neuropathic pain. Misuse seems to have increased rapidly in recent years and is a globally recognised problem, reflected in early Australian data. Misuse is more pronounced among patients with substance use disorder, particularly involving opioids. Gabapentinoids may potentiate the effects of methadone or buprenorphine/naloxone, with euphoric effects.

The exact mechanism of action is unknown. Although gabapentinoids are a structural derivative of the inhibitory neurotransmitter GABA, they do not bind directly to GABA or benzodiazepine receptors.

Pregabalin is marketed as Lyrica®.

Effects and presentation

Euphoria; dizziness, drowsiness, fatigue and somnolence; infection; ataxia; blurred vision, diplopia (double vision) and visual field loss; constipation; headache; peripheral oedema; tremor; weight gain; accidental injury; and dry mouth.

Drug interactions

Combining with opioids or other CNS depressants (e.g. benzodiazepines) increases risk of CNS and respiratory depression (respiratory failure, coma and death have been reported). Avoid combination if possible; otherwise monitor closely, lower doses may be required.

May increase the effects of alcohol.

Intoxication and overdose

There has been a rise in pregabalin-associated deaths in Australia – co-ingested opioids, benzodiazepines, alcohol and illicit drugs were much more common in fatal cases. Symptoms in overdose included affective disorder, somnolence, confused state, CNS and respiratory depression, myoclonic jerks, agitation and restlessness. Seizures were also reported.

Withdrawal

Withdrawal symptoms may occur following abrupt discontinuation of pregabalin treatment. Symptoms may include insomnia, headache, nausea, anxiety, sweating and diarrhoea. It is recommended that patients undergo a short taper period (1 week) when discontinuing treatment.

Emerging drugs of concern

Quetiapine

Overview

There is a growing number of reports of quetiapine misuse, abuse, tolerance and/or physical dependence. This includes both prescribed and diverted quetiapine by intravenous drug users. Quetiapine appears to be the most documented antipsychotic bought and sold illicitly on the street with street names 'quell', 'Susie-Q', 'baby heroin' and 'q-ball'.

Antipsychotic actions are thought to be mediated (at least in part) by blockade of dopaminergic transmission in various parts of the brain (in particular the limbic system). The mechanism for abuse potential is not fully understood. While abuse has been frequently associated with those who use or are dependent on benzodiazepines, quetiapine has no meaningful activity at benzodiazepine receptors.

Effects and presentation

Adverse effects include tachycardia and somnolence, dry mouth, weight gain, dizziness and asthenia (weakness or lack of energy).

Drug interactions

Antipsychotic and other centrally acting medicines – given the primary CNS effects of quetiapine, it should be used with caution in combination with other centrally acting medicines and alcohol.

Quetiapine is metabolised by CYP3A4 enzyme – medications that induce or inhibit this enzyme may alter the effect of quetiapine.

Quetiapine has a potential to lower seizure threshold, and risk increases when recreational users are on other medications that cause the same risk.

Intoxication and overdose

Certain effects may be more common with specific agents. A large retrospective case series found that quetiapine overdose appears more likely to cause respiratory depression, depressed mental status and hypotension compared to other antipsychotics. Most patients with quetiapine overdose do well with supportive care. Coma is not expected unless the dose ingested is beyond 2–3 g, in which case intubation may be required. QT prolongation induced by quetiapine alone is not related to Torsades de Pointes. Duration of monitoring and supportive care also depends on the formulation (immediate release vs modified release) of the tablet.

Withdrawal

Acute withdrawal symptoms such as nausea, vomiting and insomnia have been described after abrupt cessation of antipsychotic medicines including quetiapine. Cholinergic rebound syndrome (e.g. flu-like symptoms, nausea, vomiting and agitation) and activation syndrome (e.g. restless overactivity, insomnia, nausea and vomiting) have also been reported.

