Illicit drugs and anaesthesia

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Introduction

About 13.3% of South Africans meet the criteria to be diagnosed with a substance use disorder (SUD) according to the United Nations Office’s Drugs and Crime World Drug Report of 2022. The international prevalence of SUD is around 5.5% according to the World Health Organization (WHO). Compared to the rest of the world, this indicates that South Africa’s substance use problem is nearly two and a half times larger.

The understanding of addiction has undergone recent changes. SUD is now recognised as a medical disease and is no longer considered merely a symptom of poor self-control or a lack of moral fibre. Removing the stigma of addiction has improved both patient access to rehabilitation and rehabilitation success rates. Much of this shift has come about because of the opioid use disorder (OUD) epidemic in the United States, which has progressively worsened since 2017. If one considers that the prevalence of asthma and diabetes mellitus in Africa both are around 12%, then the scale of the SUD epidemic can be appreciated.

After nicotine, alcohol is the most used substance in South Africa. Following these, the list of commonly used substances in South Africa includes cannabis, methaqualone (Mandrax), 3,4-Methylenedioxymethamphetamine (MDMA, Ecstasy), cocaine, methamphetamine (crystal meth/Tik), and heroin. Newer “designer drugs” are constantly being added to the menu of options. Because nicotine and alcohol are not illicit substances, they will not be discussed here.

Classification

It is clinically useful to classify substances as stimulants, depressants, and hallucinogens. Tables I–XI below summarise these and other substances’ actions, pharmacokinetics, chemical structure, pharmacodynamics, and adverse effects.

Stimulants

Stimulants usually increase the release or block the reuptake of catecholamines.
Pharmacodynamics: Euphoria.
Increased energy levels.
Increased ability to concentrate (methylphenidate).

Adverse effects: Hypertension, tachycardia, panic attack, and paranoid psychosis.
Serotonin syndrome or rhabdomyolysis if used in conjunction with other serotonergic agents or CYP2D6 inhibitor agents. Contraindicated within 14 days of any monoamine oxidase inhibitor use. Prescription methylphenidate should be continued perioperatively to avoid haemodynamic instability from acute withdrawal.13

Table III: Methamphetamine/crystal meth (Tik).7,13
Action: Catecholamine reuptake inhibitor.
Pharmacokinetics: Administration: Oral, inhaled, or intravenous. Metabolism: Metabolised to amphetamine. Onset of action: 3 hours orally, 5–10 minutes inhaled or intravenous. Duration of action: 6–12 hours.
Chemical structure: Synthesised from ephedrine and pseudoephedrine.
Adverse effects: Physical dependence. Narrow therapeutic index for respiratory depression. Opioid-induced hyperalgesia complicates analgesia. Withdrawal can present within 6–18 hours after the last dose. Withdrawal will require oral or intravenous opioids. Agonist-antagonist agents such as nalbuphine or antagonists such as naloxone must be avoided to prevent withdrawal.13

Table IV: MDMA (Ecstasy).7,12,11
Action: Empathogen and entactogen (enhanced social connectivity). Primarily causes serotonin release into the synaptic cleft.
Chemical structure: Amphetamine.
Pharmacodynamics: Euphoria, sociability, and potential psychedelic effects.
Adverse effects: Serotonin syndrome. Fever, hyponatremia, rhabdomyolysis, renal failure, and liver failure while intoxicated. Low energy (“crash”), low catecholamine levels for days post-use.

Depressants

Table V: Heroin (diacetylmorphine).9,16,17
Pharmacokinetics: Administration: Oral, inhaled, intravenous, or subcutaneous. Absorption: Orally absorbed and then deacetylated to morphine. Metabolism: In central nervous system to monoacetylmorphine; peripherally to 6-monoacetylmorphine; metabolised in plasma, liver, and other tissues. Excretion: 90% renally cleared. Onset of action: 10-20 minutes orally, 3 minutes inhaled, 1 minute intravenous, 5 minutes subcutaneous. Duration of action: Several hours.
Chemical structure: Diacetylmorphine, a semisynthetic derivative of morphine.
Pharmacodynamics: Analgesia, sedation, and respiratory depression.
Adverse effects: Physical dependence. Narrow therapeutic index for respiratory depression. Opioid-induced hyperalgesia complicates analgesia. Withdrawal can present within 6–18 hours after the last dose. Withdrawal will require oral or intravenous opioids. Agonist-antagonist agents such as nalbuphine or antagonists such as naloxone must be avoided to prevent withdrawal.13

Table VI: Oxycodone.18
Action: Mu, kappa and delta agonist. Oxycodone: Morphine dose ratio 1:1.5–2.
Pharmacokinetics: Administration: Oral or inhaled. Metabolism: In the liver by CYP3A4 & CYP2D6 to noroxycodone and oxymorphone. Excretion: Metabolites are excreted renally. Onset of action: 10–30 minutes orally, 2-5 minutes inhaled. Duration of action: 3–6 hours.
Chemical structure: Semisynthetic opioid.
Pharmacodynamics: Analgesia, sedation, and respiratory depression.
Adverse effects: Physical dependence. Nasal septum and soft palate necrosis in patients who “snort” crushed tablets.

Table VII: Methaqualone (Mandrax).10
Pharmacodynamics: Euphoria, anxiolysis, and sedation.
Adverse effects: Withdrawal: 12–24 hours after the last dose.

Hallucinogens

Table VIII: Phencyclidine (PCP, "angel dust").9,19,20
Action: N-methyl-D-aspartate antagonist. Dopamine agonist, partial adrenergic agonist, and serotonin antagonist.
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Acute intoxication

Wherever possible, the patient who presents acutely intoxicated should be postponed until the substance has been cleared to avoid haemodynamic instability. The management of acute toxicity is largely supportive. Any additional agents required will depend on the substance involved and the clinical picture.

Stimulant intoxication will present with a sympathomimetic clinical picture, with the differential diagnosis of thyrotoxicosis, malignant hyperthermia, neurolept malignant syndrome, and opioid withdrawal. In the case of toxicity from stimulants, acute central nervous system and cardiovascular system toxicity can be managed with a variety of agents. Dexmedetomidine (alpha-2 agonist) has recently gained popularity for this role. Other commonly used agents include benzodiazepines, direct-acting vasodilators, calcium channel blockers, and mixed alpha and beta antagonists. The use of selective beta blockers, which would leave the patient exposed to unopposed alpha stimulation, is controversial and generally not recommended. The successful use of intravenous lipid emulsion to counteract the toxicity of lipid-soluble agents, such as psychotropic agents and cocaine, is also described.

In the case of a depressant substance toxicity, the management is again supportive, (especially in terms of respiratory depression) with the additional options of naloxone and flumazenil as antidotes for opioids and benzodiazepines, respectively.

Acute withdrawal

The clinical picture will depend on whether the patient is suffering withdrawal from a stimulant or a depressant agent. The patient may present with a spectrum from mild tremors, fever, and electrolyte derangement to haemodynamic instability, altered consciousness, and seizures. Psychostimulant agent withdrawal may present with depression, a decreased consciousness level, lethargy, and haemodynamic depression or potentially with anxiety, agitation, and psychosis.

Dexmedetomidine and benzodiazepines form the mainstay of the management of withdrawal from depressant agents such as alcohol or opioids in conjunction with further supportive management, such as inotropic support where required.
**Chronic SUD**

All patients presenting for surgery, including the SUD patient, must be assured that they will be offered adequate and appropriate analgesia. The 2022 Centers for Disease Control and Prevention (CDC) clinical practice guideline recommends the maximised use of multimodal analgesic agents and regional techniques to reduce opiate requirements as much as possible in chronic SUD patients. However, where necessary, it is not recommended to withhold opiates. The use of opioids in these patients should be at the lowest effective dose and for the shortest required duration. These patients may exhibit hyperalgesia and it may be difficult to control their pain with opioids alone. Hence the recommendation is to use multimodal analgesia, including regional techniques, as far as possible. Where opioids are used, the more potent, shorter-acting agents are recommended. If opioids are used for longer than a few days, their dose should be tapered and not stopped abruptly.

A patient being rehabilitated for OUD may present for surgery on methadone (Table XII) or buprenorphine (Table XIII). It is recommended that these are continued through the perioperative period. The SUD patient may also present additional challenges, such as difficult intravenous access, a difficult airway, an altered level of consciousness, and a stormy haemodynamic perioperative course.

The chronic cocaine SUD patient may present with catecholamine depletion and fewer postsynaptic receptors, which require the use of higher doses of direct-acting vasopressors or inotropes, as indirect-acting agents will not be able to facilitate the release of endogenous catecholamines. Refractory hypotension in these patients may require the use of vasopressin.  

**Medications for OUD**

**Table XII: Methadone**

<table>
<thead>
<tr>
<th>Action</th>
<th>Mu agonist and N-methyl-D-aspartate receptor antagonist. Also, serotonin and noradrenaline reuptake inhibitors. Prescribed for chronic opioid rehabilitation in patients with OUD and for chronic pain patients.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical structure</td>
<td>Synthetic opioid.</td>
</tr>
<tr>
<td>Pharmacodynamics</td>
<td>Analgesia.</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>Withdrawal begins 24–48 hours after the last dose. Prolonged QT and possible torsade de points. Respiratory depression in overdose, may be lethal in combination with other sedative/depressant agents.</td>
</tr>
</tbody>
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**Table XIII: Buprenorphine**

<table>
<thead>
<tr>
<th>Action</th>
<th>Opioid agonist-antagonist (partial mu agonist, kappa antagonist).</th>
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<tbody>
<tr>
<td>Chemical structure</td>
<td>Morphin alkaloid.</td>
</tr>
<tr>
<td>Pharmacodynamics</td>
<td>Potent analgesia with less respiratory depression and euphoria.</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>Nausea, vomiting, drowsiness, orthostatic hypotension, and urinary retention.</td>
</tr>
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**Conclusion**

Managing a SUD patient in the perioperative space requires an understanding of the potential effects and drug interactions of the substance used. It is a valuable contact time for postoperative referral for counselling, but not the time for rehabilitation. Furthermore, inadequately managing a patient’s pain may do more harm and potentially push a recovering SUD patient to relapse.

**References**