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Recreational drugs and implications for anaesthesia

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Introduction

South Africa is increasingly becoming recognised as an important international drug centre. This is in terms of production, transport**,** as well as usage of illicit substances. In addition to the local production of significant amounts of marijuana and methaqualone ("Mandrax"), South Africa is also becoming more and more popular as an international transport hub for foreign-produced substances.[1] These include cocaine from South America and heroin from Afghanistan, bound for Europe, North America and the rest of Africa.[1]

While absolute figures for substance abuse are difficult to measure, it is estimated that the South African national numbers for substance abuse are at least twice that of the rest of the world. According to the World Health Organisation (WHO) and the United Nations Office on Drugs and Crime (UNDOC), the incidence of substance abuse worldwide varies between 3.5%-5.7%.[1] According to the Central Drug Authority (CDA) of South Africa, it is estimated that the incidence in South Africa is around 15%.[2] In addition to the full array of agents available internationally, we have our own home-grown unique problems in the forms of "Tik", "Nyaope" or "Wunga", as well as "Mandrax".

Anaesthetists in South Africa therefore have a very high probability of encountering patients who have been exposed to some form of substance abuse. Patients may present from all walks of life, for emergency or elective surgery, having abused a single agent or a mixed cocktail of drugs, intoxicated or rehabilitated. We should also not forget that the non-illicit substances, nicotine and alcohol, remain the two most abused substances ahead of all the illicit substances available.

"Legal highs" and "designer drugs" also exist. These agents may not be illegal initially, but their psychological side-effects are eventually uncovered by health or law enforcement authorities. They are often "forgotten" pharmaceuticals which were abandoned in development, sometimes for such diverse indications as weight loss or anti-helminthics. Most commonly these agents have amphetamine-like properties. Some are specifically designed for the drug trade, usually to be analogues of amphetamines, producing euphoria and empathy ("Empathogens").[3]

The ratio of men to women who abuse drugs is 2:1. Men are more likely to abuse marijuana, cocaine and amphetamines. Women are more likely to abuse prescription drugs, notably opioids and tranquilisers. Women are less likely to receive treatment for drug abuse than men, with only one woman receiving treatment for every four men in rehabilitation programmes.[1]

Classification

The ultimate aim of most substance abuse is to "get high" by altering dopamine levels in the mesolimbic (reward) area of the brain.[4,5,6] Pathways to achieving this may be direct or indirect and usually involve many other receptor systems, either by design or as an unintended consequence. (Dopamine, Serotonin, Adrenaline, Noradrenaline, μ, GABA, NMDA, nicotinic and histamine receptors may all be stimulated in the process). Some agents may act at several receptor sites.[3] To sift through the ensuing pharmacological "soup"; it is useful clinically, to divide substances into three categories, based on their cardio-respiratory and neurological effects:

1. "Uppers":

   These include cocaine, amphetamines and their derivatives such as MDMA (3, 4-methylenedioxymethamphetamine or "Ecstasy") and methamphetamines. "Uppers" usually function by raising intra-synaptic catecholamine levels and may present with a phaeochromocytoma or serotonin syndrome type clinical picture.

2. "Downers": (Stimulate μ or GABA receptors).

   These include opiates, benzodiazepines and cannabis. Opiate abuse is responsible for more than 90% of the accidental deaths which occur related to drug overdose and abuse.[3] Opiates are commonly abused for the feeling of euphoria which they elicit.

3. Hallucinogens: (Stimulate NMDA and serotonin receptors). This group includes Lysergic acid diethylamide (LSD), Phencyclidine (PCP) and Ketamine.

It is important to remember though, that patients may present having taken a "cocktail" of various substances, often from

different classes and often including alcohol. This could seriously cloud the clinical picture.

RSA top nine:[7]

The most commonly abused substances in South Africa are as follows:

1. **Nicotine**

2. **Alcohol**

3. **Cannabis**

   The active ingredient is Delta-9-tetrahydrocannabinol (THC).

   THC alone usually causes sedation, which may have an unpredictable interaction with general anaesthesia. It may however also cause acute agitation, which if necessary**,** may be treated with benzodiazepines or an alpha 2 agonist. In general marijuana tends to increase the stimulatory or depressant effects of "uppers" or "downers" if taken together with either.[8] Marijuana smoke causes more carbon monoxide and tar build–up as well as greater airway irritation than tobacco smoke does, which may be especially problematic if the patient has smoked recently prior to anaesthesia. Other potential complications are tachycardia, postural hypotension and seizures.[3]

4. **Mandrax (Methaqualone)**

   This is a synthetic "downer" agent, originally prescribed for insomnia. South Africa has the highest production and abuse figures in the world.[7, 9] Mandrax tablets are usually crushed and smoked, either with cannabis or tobacco. This agent is physically and psychologically addictive.[9]

5. **Ecstasy (3, 4-methylenedioxymethamphetamine MDMA)** [3]

   This is a synthetic, indirect acting sympathomimetic agent with central nervous system (CNS) stimulating effects. MDMA causes increased secretion and decreased re-uptake of intra-synaptic noradrenaline, dopamine and serotonin, leading to feelings of euphoria and extreme empathy. ("Love drug"). Hyperpyrexia and the serotonin syndrome may occur. Ecstasy may also cause a prolonged QT interval. Post-use there is extreme depletion of pre-synaptic catecholamine stores. Treatment of acute intoxication and overdose is supportive, with careful monitoring of fluid and electrolyte status necessary. Hypertension and tachycardia should be managed with a non-selective beta blocker and hypotension will require the use of a direct acting vasopressor.

6. **Cocaine**[3, 10, 11]

   A natural alkaloid, extracted from the coca plant, originally of South America. Cocaine is a water soluble hydrochloride salt, which may be taken orally, nasally or intravenously.

   Bioavailability is 30-40% if taken per os and 80-90% inhaled or intranasal.

   Cocaine inhibits the pre-synaptic re-uptake of dopamine, noradrenaline, adrenaline and serotonin.

   This leads to sympathetic stimulation with cardiovascular, respiratory, central nervous system and renal stimulation. The seizure threshold is decreased. Hypertension and tachycardia are common, with significant potential for dysrhythmias and myocardial ischemia.[3] Because cocaine leads to both alpha and beta adrenergic stimulation, it is important to not treat hypertension and tachycardia with a pure beta blocker. This could lead to unopposed alpha stimulation. Vasodilators which cause a reflex tachycardia could also worsen an acute intoxication picture. Dexmedetomidine may be the drug of choice to control sympathetic overstimulation by providing alpha blockade and central sedation. If hypotension should occur under anaesthesia, a direct acting vasopressor would be a more prudent choice as there may be pre-synaptic catecholamine depletion.[3, 8]

   Cocaine also has a local anaesthetic effect, by blocking sodium channels. This may lead to prolongation of the QRS complex, negative inotropy and negative chronotropy.

7. **Crack**[3]

   Crack is a free base form of cocaine which is smoked. It is more potent and has a faster onset of action than cocaine.

8. **Methamphetamine/ Crystal meth (TIK)**[8,10]

   These are derivatives of amphetamines (see below), which cause an increased synaptic release of adrenaline, noradrenaline, serotonin and dopamine. They may be taken nasally, orally, intravenously or smoked. An electrocardiogram (ECG), and if time warrants, an echocardiogram should be requested on all chronic users preoperatively as chronic use may cause acute coronary syndrome, cardiomyopathy and even aortic dissection.[8]

   "TIK" is a combination of crystal methamphetamine and some other white powder to "cut" or increase the bulk of the product. This "cutting" agent includes anything from detergents or pesticides to heroin. (Heroin is often added to increase the addictiveness). "Tik" is smoked in a glass pipe called a "Lolly". It has also been called "Hitler's drug" because it was originally designed during the Second World War for use by Nazi soldiers. The aim was to increase the soldiers' alertness and performance as well as aggression levels. This increased aggression is the main difference from other amphetamine derivatives like "Ecstasy" (a so-called "Love drug") which increase feelings of goodwill to other people. The aggression makes this a particularly difficult agent to cope with from a social point of view in affected communities.

9. **Heroin (Diacetylmorphine)**

   Heroin is a morphine derivative which is highly addictive. It may be injected, smoked or taken intranasal. Heroin causes euphoria and cardiorespiratory depression.

Other common agents of abuse:

1. **Phencyclidine (PCP)**[10]

   A hallucinogenic agent, also called "Angel dust". PCP powder is usually inhaled and produces a dissociative state.

   Ketamine is a derivative of PCP.

2. Benzodiazepines

Usually obtained by legal prescription.

3. Oxycodone

Also usually obtained by legal prescription.

4. Amphetamines

A group of agents with many derivatives. As a group these drugs are all indirectly acting sympathomimetic agents which cause pre-synaptic release and inhibition of re-uptake of adrenaline, noradrenaline, serotonin and dopamine. These agents have a chemical structure similar to that of adrenaline and dopamine.

5. Methadone

A μ agonist and NMDA receptor antagonist, which also causes some noradrenaline and serotonin re-uptake inhibition. This synthetic opioid is commonly prescribed in the management of chronic pain and also to enable rehabilitation from opiate addiction by preventing opiate withdrawal. Methadone has a rapid onset of action and three times greater bioavailability than morphine when taken per os. Methadone has a long half-life, of around 24 hours, allowing once daily dosing. It can cause prolonged QT-syndrome, which may lead to Torsade's des Pointes in overdose.[9]

6. Flunitrazepam[9, 11]

A benzodiazepine called "Rohypnol". Leads to anterograde amnesia and sedation. Has been used as a "Date-rape" drug.

7. Gamma hydroxybutyrate (GHB) [9, 11]

This is a metabolite of GABA which was originally used for narcolepsy. It produces a brief period of euphoria followed by coma. GHB has also been used as a "Date-rape" drug.

8. Solvents. ("Glue sniffing")[12, 13]

Various volatile agents can be "sniffed" from a plastic bottle or bag. Usually glues, cleaning agents or fuels. Physical dependence is rare, but psychological dependence and tolerance are common. May lead to cardiovascular, pulmonary and renal complications as well as acute methaemoglobinaemia.

9. Methylphenidate. ("Ritalin")[14, 15]

This is a derivative of the amphetamine group. It causes an increase in alertness and concentration.

It is usually prescribed for children suffering from attention deficit hyperactivity disorder (ADHD).

It is abused by students and professionals to increase productivity. Methylphenidate causes an increase in dopamine levels in the mesolimbic region of the brain which raises the concern that it may worsen mood disorders like bipolar syndrome in susceptible people. There is also concern that it may be a "gateway drug". It has been called "Kiddie-coke" or "Coke-light".

10. Nitrous Oxide

A recent trend of nitrous oxide abuse has emerged in countries like the Netherlands and the UK. Nitrous oxide is usually obtained from catering sources such as cream-foamer "bombs". This is then transferred to balloons from which it is then inhaled. Acute complications are mainly trauma-related from loss of consciousness and subsequent injuries. Chronic complications are peripheral neuropathies from vitamin B12 deficiency due to interference with homocysteine metabolism.[20]

11. "Nyaope" and "Wunga"

Nyaope:

This is a mixture of Marijuana and Heroin rolled into a "joint" and smoked. The Heroin may include several bulking agents like detergents, pesticides etc. (E.g. "VIM, "RATTEX") as well as other "muti" type ingredients.

Wunga:

Wunga is Nyaope taken a step further by adding the antiretroviral (ARV) agent Efavirenz. Efavirenz causes an LSD type of hallucinogenic side-effect by stimulating 5-HT2A serotonin receptors.[16] This was discovered by South African patients on ARVs, who subsequently began experimenting by crushing the tablets and smoking the powder[17]. This has led to antiretroviral (ARV) drugs developing a "street-value" with patients selling their medication as well as clinics etc. being burgled for their ARVs. It has also raised concern about immunity developing against ARVs if they are widely abused, particularly as some poorly informed abusers may not be able to discriminate between different ARVs , and add any or all to the cocktail.

Anaesthetic considerations:

- If a patient presents for surgery acutely intoxicated and/ or following an overdose, then it is prudent to delay surgery and anaesthesia for as long as is safely possible, to avoid the serious risk of haemodynamic instability.[8] These patients may have a mix of several agents, including alcohol on board, which could complicate their management. It is worth having a high index of suspicion that they may be presenting with depleted catecholamine stores. By delaying and optimising these patients, they will benefit from having fewer drug interactions and a lesser incidence of withdrawal syndromes. In the case of cocaine use, it is recommended to wait at least one week before embarking on elective surgery.[13]
- The recovering addict presenting for anaesthesia.[10,18]
- Attempt to use multimodal and regional anaesthesia where this is possible.
- Avoid opiates only if it is feasible to do so however.[10,18] Adequate analgesia may require opiates, which may be needed at higher doses than normal. Opiates given for actual pain do not lead to addiction or relapse. Inadequate analgesia in itself however, may actually provoke a relapse to addiction.[18]
- Avoid opiate antagonists, e.g. Nalbuphine which may precipitate a withdrawal response.[8]

- Have a high index of suspicion for substance abuse in all acute trauma patients.
- Alcohol withdrawal and Delirium Tremens (DTs) may occur at any stage perioperatively, and may be life-threatening. Signs and symptoms may vary from mild tremors, confusion and pyrexia to electrolyte disturbances, haemodynamic instability and seizures.[8, 19]
- "Meth mouth" may be present when inhaled agents are abused. This typically presents with poor oral hygiene and loose or missing teeth. This is often a contributing factor to the patient's poor nutritional status.[8]
- A perforated nasal septum as well as soft palate destruction, from chronic cocaine "snorting" may make bag-mask ventilation and intubation difficult.
- Pulmonary toxicity with ensuing pulmonary hypertension may be present, mostly from chronic inhaled substance or sympathomimetic agent abuse. The addition of toxic "cutting" agents to dilute the powder form of drugs may exacerbate this problem.[8, 11]
- The patient may display poor general hygiene and suffer from a poor general nutritional status.[11]
- Difficult intravenous access may be a problem[8].
- Altered pain perception. Hyperalgesia may be a problem, especially in chronic opiate abuse.[8]
- Patients who are intravenous drug abusers tend to suffer from a higher incidence of Hepatitis B, HIV and infective endocarditis.[11]
- Always maintain a high index of suspicion for a potential drug and/or alcohol withdrawal phase, which could be fatal if untreated.

Antidotes:

- Naloxone:

  This is a μ receptor antagonist, which is occasionally prescribed as a "take-out" prescription (TTO) abroad. Naloxone is however controversial for acute use as it may lead to a severe withdrawal syndrome or myocardial ischemia, especially if given in a rapid large bolus.[11]

- Anexate:

  Benzodiazepine antagonist.

- Intravenous Lipid Emulsion (ILE): [3]

  Renal dialysis can easily remove molecules which are large and water soluble. Most illicit substances of abuse are however, small and highly lipid soluble molecules. This allows them to cross the blood brain barrier easier. To decrease the effective plasma concentration of these molecules, the best option is thus to increase their volume of distribution. To do this, the patient may be exposed to a dose of ILE, which acts as a "Lipid sink".

- Dexmedetomidine (α 2 agonist).[3, 8]

  Dexmedetomidine is centrally sedating and sympatholytic. It has been shown to be useful in managing the hypertension and CNS excitation in opiate and particularly cocaine withdrawal. It is also very useful for managing acute intoxication or overdose of "upper" agents. (Dose 0.1-0.3 μg/kg).

Conclusion

Substance abuse appears to be a far more common problem in South Africa than in many other countries worldwide. Patients may present from all walks of life with a wide variety of of clinical pictures. It is important to always maintain a high index of suspicion that a patient may have been exposed to some form of recreational drug abuse.

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