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اسم المادة باللغة العربية: السموم السريرية

اسم المادة باللغة الإنكليزية: **Clinical toxicology**

المرحلة: الخامسة

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عنوان المحاضرة باللغة العربية: إساءة استخدام الادوية.

عنوان المحاضرة باللغة الإنكليزية: **Drugs abuse**

Drugs abuse

Substance abuse, also known as **drug abuse**, is a patterned use of a drug in which the user consumes the substance in amounts or with methods which are harmful to themselves or others.

Drugs of abuse are classified according to their action into:

1. **Psychomotor stimulants cause:**
    - Excitement
    - Euphoria
    - Decrease feeling of fatigue
    - Increase motor activity

E.g. Methylxanthines (caffeine, theobromine, theophylline), nicotine, cocaine, amphetamine, atomoxetine, modafinil, and methylphenidate.

2. **Hallucinogens (psychotomimetic)**

Affect thought, perception, and mood, therefore produce

- Profound changes in thought patterns and mood
- Little effect on the brain stem and spinal cord.

E.g. Lysergic acid diethylamide (LSD), phencyclidine (PCP), tetrahydrocannabinol (THC), and rimonabant.

1. Psychomotor stimulants

a. Cocaine: (highly addictive drug)

Mechanism of action:

- Blockade of reuptake of the monoamines (NE, serotonin and dopamine).Thus potentiates and prolongs the CNS and peripheral actions of these monoamines.
- Initially produces the intense euphoria by prolongation of dopaminergic effects.
- Chronic intake of cocaine depletes dopamine. This depletion triggers the craving for cocaine that temporarily relieves severe depression.

Adverse effects:

- ✓ Anxiety reaction that includes:

  Hypertension

  Tachycardia

Sweating

Paranoia

- ✓ Cocaine chest pain can also be due to pulmonary damage caused by inhaling this hot impure substance.
- ✓ Cocaine convulsions are a natural extension of the CNS stimulant effect.
- ✓ Because of the irritability, many users take cocaine with alcohol. A product of cocaine metabolites and ethanol is **cocaethylene**, which is also psychoactive and cause cardiotoxicity.
- ✓ Depression, like all stimulant drugs, cocaine stimulation of the CNS is followed by a period of mental depression.
- ✓ Addicts withdrawing from cocaine exhibit physical and emotional depression as well as agitation.

Treatment:

- ➢ Cocaine toxicity is treated by calming and cooling the patient.
- ➢ Benzodiazepines such as lorazepam, help to calm the agitated patient and can both treat and prevent convulsions
- ➢ Seizures treated with IV. Diazepam.
- ➢ In addition, the calming effect helps cool the patient and manage the hyperthermia. This is an important effect, as hyperthermia is one of the major causes of cocaine fatalities.
- ➢ The remainder of cocaine toxicity is treated with short acting anti-hypertensives, anticonvulsant, and symptomatic supportive care.
- ➢ Fatal cardiac arrhythmias.→→propranolol.

b. Amphetamine:

- Is a non- catecholamine (show neurologic and clinical effects quite similar to those of cocaine).
- Dextroamphetamine is a major member of this class compounds.
- Methamphetamine is a derivative of amphetamine that can be smoked and it is preferred by many abusers.
- Methylenedioxymethamphetamine (MDMA) is a synthetic derivative of methamphetamine with both stimulant and hallucinogenic properties.

Adverse effects:

- The amphetamines may cause addiction, dependence, tolerance, and drug seeking behavior.
- CNS adverse effects: insomnia, irritability, dizziness, tremor, confusion, delirium, panic states, and suicidal tendencies, especially in mentally ill patients.
- Chronic amphetamine use produce a state of "amphetamine psychosis" that resembles the psychotic episodes associated with schizophrenia. Whereas long term amphetamine is associated with psychic and physical dependence, tolerance to its effects may occur within a few weeks.

Treatment:

- ABC (administer oxygen, obtain IV access, assess blood glucose level)
- Monitor the patient, and perform frequent vital sign checks and serial assessment of consciousness.
- In acute toxicity, perform gastrointestinal decontamination by administering activated charcoal.
- Oro-gastric lavage usually is not necessary unless a life- threatening is involved and the patient presents within 1 hour of ingestion.
- Whole bowel irrigation may be indicated.
- Anxiety, extreme agitation, panic reactions, and seizures may require short- acting BZ (e.g. lorazepam).
- Overdoses are treated with chlorpromazine or haloperidol which relieve the CNS symptoms.
- Patient presenting with sever hyperthermia require aggressive cooling measures and adequate fluid resuscitation.
- Morbidity is directly related to the severity and duration of hyperthermia.
- Cardiac monitoring and an electrocardiogram in patients complaining of chest pain or palpitation.

2. Hallucinogens (psychotomimetic)

a. Lysergic acid diethylamide (LSD)

- Multiple sites in the CNS are affected by LSD.

- The drug shows serotonin (5-HT) agonist activity at presynaptic 5-HT1 receptors in the midbrain, and also stimulate 5-HT2 receptors.
- Activation of the sympathetic nervous system occurs, which cause pupillary dilation, increased blood pressure, piloerection, and increased body temperature.

Adverse effects:

- Hyperreflexia
- Nausea
- Muscular weakness
- High doses may produce long lasting psychotic changes in susceptible individuals.

Treatment:

Haloperidol and other neuroleptic can block the hallucinatory action of LSD and quickly abort the syndrome.

b. <u>Tetrahydrocannabinol (THC)</u>

The main psychoactive alkaloid contained in marijuana is tetrahydrocannabinol which is available as **dronabinol**.

Adverse effects:

- TCH can produce euphoria, followed by drowsiness and relaxation.
- Affect short-term memory and mental activity.
- Decreases muscle strength
- Impairs highly skilled motor activity, such as that required to drive a car.
- Appetite stimulation, xerostomia, visual hallucination, and delusion.

Therapeutic uses of <u>dronabinol</u> as:

- An appetite stimulant for patients with acquired immunodeficiency syndrome who are losing weight.
- It is also sometimes given for the sever emesis caused by some cancer chemotherapeutic agents.

c. <u>Rimonabant</u>

- The cannabinoid receptor CB1 antagonist.
- It is an anorectic anti –obesity drug (decrease appetite and body weight in humans).

- Induce psychiatric disturbances, such as anxiety and depression during the clinical trials.

d. Phencyclidine:

- Phencyclidine (also known as PCP, or angel dust) inhibits the reuptake of dopamine, 5HT and norepinephrine.
- Phencyclidine, an analog of ketamine, causes dissociative anesthesia (insensitivity to pain, without loss of consciousness) and analgesia.
- At increased dosages, anesthesia, stupor, or coma result, but the eyes may remain open.
- Increased sensitivity to external stimuli exists, and the CNS actions persist for a week.

3. Other drugs of abuse:

a. Opioid Abuse

- Symptoms vary according to level of intoxication. For mild to moderate intoxication, individuals may present with drowsiness, pupillary constriction, and slurred speech. For severe overdose, patients may experience respiratory depression, stupor, and coma. A severe overdose may be fatal.

- **Tolerance** is the need for increasing doses of medication to achieve the initial effect of the drug. Tolerance to the analgesic and euphoriant effects and unwanted adverse effects, such as respiratory depression, sedation, and nausea, may develop. However, little tolerance develops to constipation and meiosis.

- Continuous administration of opioids leads to physical dependence. Physical dependence is expected after 2-10 days of continuous use when the drug is stopped abruptly. The onset and duration of withdrawal varies with the drug used.
- For example, meperidine withdrawal symptoms peak in 8-12 hours and last for 4-5 days. Heroin withdrawal symptoms usually peak within 36-72 hours and may last for 7-14 days.

Symptoms of <u>withdrawal</u> include the following:

1. Autonomic symptoms - diarrhea, rhinorrhea, diaphoresis, lacrimation, shivering, nausea, emesis, piloerection
2. Central nervous system arousal - sleeplessness, restlessness, tremors
3. Pain - abdominal cramping, bone pains, and diffuse muscle aching
4. Craving - for the medication

- **<u>Addiction</u>** is characterized as a psychological and behavioral syndrome in which the following features are observed:

1. Drug craving
2. Strong tendency to relapse after withdrawal

<u>Management</u>

General supportive measures for **<u>opioid intoxication</u>** are as follows:

- Assess patient to clear airway.
- Provide support ventilation, if needed.
- Assess and support cardiac function.
- Provide IV fluids.
- Frequently monitor the vital signs and cardiopulmonary status until the patient has cleared opioids from the system.
- Give IV naloxone if necessary, it rapidly reverses the respiratory depression and sedation caused by heroin intoxication.

Pharmacologic therapy for **<u>heroin addiction</u>** has focused on ameliorating withdrawal symptoms and reducing cravings. By replacing heroin with legally obtained opioid agonists, many risk factors of the drug-abusing lifestyle can be mitigated.

1. Methadone, a long-acting synthetic opioid agonist, can be dosed once daily and replaces the necessity for multiple daily heroin doses.
   (Long-acting medications, such as methadone and sustained-release morphine, tend to have slower onset of action. Thus, the longer-acting opioids are less likely to be abused).

2. Buprenorphine is a mu-opioid partial agonist that, like methadone, suppresses withdrawal and cravings.

b. Sedative/ hypnotic drugs:

Barbiturate and benzodiazepines

- Both groups may induce psychological and physical type of dependence (markedly more likely, sever, and earlier onset in barbiturates)
- Withdrawal syndrome: nervousness, restlessness, tremor, anxiety, confusion, dizziness, delirium, and convulsion.
- Risk of acute intoxication and respiratory depression is much greater with barbiturates, BZ are safer but sever cases often appear when they are combined with alcohol.

c. Solvents:

- Different lipophilic organic solvents acts as unspecific narcotics (e.g. toluene, acetone)
- Route of administration →→ inhalation
- In lower doses →→euphoria, pseudo hallucination, and pleasant dreams.
- High doses →→ profound CNS depressant effect, coma, and respiratory failure.
- Chronic abuse →→ neurodegeneration with behavioral and mental disturbance.