Al-Mustaqbal University
College of Pharmacy
5th stage
Clinical Toxicology
Lecture: 7

Abused Substances Toxicity(Cannabinoids)

Dr.Iman Ghanim

Dr,Weaam J. Abbas

Cannabinoids Toxicity

Cannabinoids Toxicity

- ✓ ***Cannabis sativa*** **is the plant from which marijuana and cannabinoids are derived.**
- ✓ **The most potent form of this plant's extracts is hash oil (a liquid).**
- ✓ **The dried flowers tops and leaves are smoked as a cigarette.**

Cannabinoids Toxicity

- ✓More than **400 active compounds** have been isolated from the *Cannabis sativa* plant.
- ✓**Sixty active compounds** are unique to the plant and are collectively known as **cannabinoids**.
- ✓**Delta-9-tetrahydrocannanbinol** (THC) is the most **psychoactive** cannabinoid, producing euphoria, relaxation, diminished pain, and difficulties with memory and concentration.

Cannabinoids Toxicity

✓**Cannabis is available in the following forms:**

1. **Marijuana is a combination of the *Cannabis sativa* flowering tops and leaves, the THC content is 0.5-5%.**
2. **Hashish is dried resin collected from the flowering tops, the THC concentration is 2-20%.**
3. **Hash oil is a liquid extract; it contains 15% THC.**
4. **Sinsemilla is without seedd - unpollinated flowering tops. THC content is as high as 20%.**
5. **Dutch hemp (Netherwood) has a THC concentration as high as 20%.**

Cannabinoids Absorption

- ✓The route of administration determines the absorption of the cannabis product.
- ✓Smoking – Onset of action is rapid (within minutes); it results in 10-35% absorption of the available THC; peak plasma concentrations occur within 8 minutes.
- ✓Ingestion – Onset occurs within 1-3 hours; 5-20% is absorbed due to stomach acid content and metabolism; peak plasma levels occur 2-6 hours after ingestion.

Cannabinoids Toxicity Pathophysiology

- ✓The specific cannabinoid receptors were discovered, **CB1 and CB2**.
- ✓The **CB1 receptors** are predominantly located in the **brain areas** responsible for anxiety, pain, sensory perception, motor coordination, memory, movement and endocrine function. This distribution is consistent with the clinical effects obtained by cannabinoids.
- ✓The **CB2 receptor**, is located **peripherally**. Specifically, it is involved in the immune system (macrophages, T and B lymphocytes), peripheral nerves.

Cannabinoids Toxicity Pathophysiology

- ✓**Both the CB1 and CB2 receptors inhibit adenylate cyclase and stimulate potassium channels. (endocannabinoid system)**
- ✓**As a result, the CR1 receptors inhibit the release of several neurotransmitters, including acetylcholine, glutamate, norepinephrine, dopamine, serotonin, and gamma–aminobutyric acid (GABA).**
- ✓**CR2 receptor signaling is involved in immune and inflammatory reactions.**

Signs and symptoms of Cannabinoids Toxicity

Behavioral effects:

- ✓**THC produces euphoria, relaxation, laughter, talkativeness, decreased anxiety, decreased alertness, and depression.**
- ✓**<u>These effects depend on the dose and mode of administration.</u>**

Mental effects:

- ✓**Short-term memory is impaired.**

Signs and symptoms of Cannabinoids Toxicity

Cardiovascular effects:

- ✓ **Rise in heart rate, lasting up to 2-3 hours.**
- ✓ **Peripheral vasodilatation causes postural hypotension, which may lead to dizziness or syncope.**
- ✓ **Cardiac output increases by as much as 30%**
- ✓ **In addition, the cardiac oxygen demand is also increased.**
- ✓ **Tolerance to these effects can develop within a few days of use.**

Signs and symptoms of Cannabinoids Toxicity

Immune system effects:

- ✓ **Cannabis use can impair the immune system's ability to fight microbial and viral infection.**

Psychosis association:

- ✓ **Large doses of THC may produce confusion, amnesia, delusions, hallucinations, anxiety, and agitation.**

Treatment of Cannabinoids Toxicity

- ✓**Immediate management should be supportive, including cardiovascular and neurological monitoring, and placement in a quiet room.**
- ✓**Gastric decontamination may be considered with an acute ingestion less than 2 hours prior to presentation.**
- ✓**Patients who are agitated or with psychosis should be treated with benzodiazepines.**

FDA NEWS RELEASE

FDA, FTC Continue Joint Effort to Protect Consumers Against Companies Illegally Selling Copycat Delta-8 THC Food Products

FDA, FTC Issue Warning Letters to Companies Selling Food Products Containing Delta-8 THC That Mimic Chips, Candies and Snacks from Popular National Brands

More Press Announcements

For Immediate Release: July 16, 2024

Lysergic Acid Diethylamide (LSD) Toxicity

✓**LSD** is one of the most potent **psychoactive**

Lysergic Acid Diethylamide (LSD) Toxicity

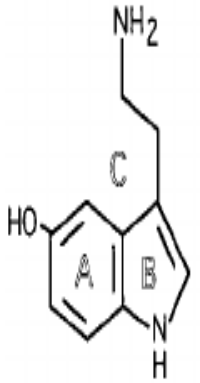
- ✓**LSD is one of the most potent psychoactive compounds was used as a psychotherapy in 1950's.**
- ✓**An oral dose of 25 µg is capable of producing potential psychological effects.**
- ✓**The drug is odorless, colorless, and slightly bitter tasting and water-soluble substance.**
- ✓**It is usually taken by mouth and rapidly absorbed by the gastrointestinal tract.**
- ✓**LSD toxicity can lead to respiratory arrest, coma, emesis, hyperthermia, autonomic instability, and bleeding disorders.**

Lysergic Acid Diethylamide (LSD) Toxicity

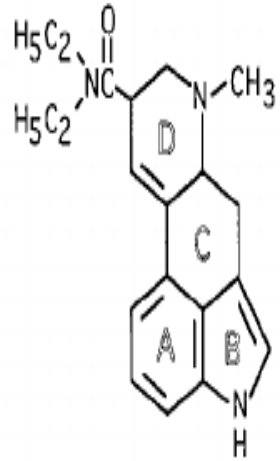
- ✓**LSD causes changes in thought, mood, and perception, with minimal effects on memory and orientation.**
- ✓**The drug primarily produces pseudohallucinations. True hallucinations occur as well; visual hallucinations are the most common.**
- ✓**In general, hallucinogens can intensify the patient's current mood; pleasant feelings can be augmented to euphoric ones, with an expanded consciousness.**
- ✓**Negative feelings or depressive symptoms can be amplified to a dysphoric experience.**

LSD Pathophysiology

- ✓The **most common route** of exposure to LSD is **oral**; the drug is absorbed **rapidly** from the **GIT**.
- ✓**Because of their structural similarity to serotonin and their intrinsic potency, hallucinogens disrupt the balanced functioning of the serotonin system.**
- ✓**Hallucinogens have a high affinity for serotonin**
- ✓**(5-HT) receptors, at which LSD exhibits agonist and antagonist properties.**



5-HT



LSD

LSD Pathophysiology

✓**The 5-HT2A receptor plays a major role in the modulation of sensory signals of the prefrontal cerebral cortex,**

where hallucinogens have effects on

cognition,

mood, perception,

and emotions ranging from fear to euphoria.

✓**These receptors are also thought to be responsible for the pathology and therapy of schizophrenia.**

LSD Pathophysiology

✓**Serotonin receptors** also important for **sensory modulation** and are **responsible** for the **sympathomimetic effects** of the drug (hypertension, tachycardia, dizziness, loss of appetite, dry mouth, sweating, nausea, numbness, tremor).

✓LSD also **stimulates dopamine (D2) receptors**, this leads to a **biphasic** pharmacologic pattern of :

1. **Early serotonin like effects** (15-30 min after administration)
2. **Late mediated dopamine like** effects (60-90 min after administration).

LSD Toxicity Management

- ✓The basic rule of management is reassurance in a safe, calm and stress-free environment.
- ✓Rarely, patients need to be either sedated or physically restrained.
- ✓Benzodiazepines can safely be given to treat agitation.
- ✓Massive ingestions of LSD should be treated with supportive care, including respiratory support and endotracheal intubation if needed.

LSD Toxicity Management

✓**The following should be treated symptomatically:**

1. **Hypertension**
2. **Tachycardia**
3. **Hyperthermia**
4. **Hypotension - Should be treated initially with fluids and subsequently with pressors if required**

THANK YOU
FOR YOUR ATTENTION