OPIOID USE DISORDERS

COURSE-PSYCHOPATHOLOGY, CC-7, Unit 4; Sem II
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Dried exudate obtained from unripe seed capsules of Papaver somniferumhas been used and abused for centuries. The natural alkaloids of opium and their synthetic preparations are highly dependence producing.

OPIOID DEREVATIVES

Natural Alkaloids of Opium

- 1. Morphine
- 2. Codeine
- 3. Thebaine
- 4. Noscapine
- 5. Papaverine

OPIOID DEREVATIVES

- B. Synthetic Compounds
- 1. Heroin
- 2. Nalorphine
- 3. Hydromorphone
- 4. Methadone
- 5. Dextropropoxyphene
- 6. Meperidine (Pethidine)
- 7. Cyclazocine
- 8. Levallorphan
- 9. Diphenoxylate

In the last few decades, use of opioids has increased markedly all over the world. India, surrounded on both sides by the infamous routes of illicit transport, namely the Golden Triangle (Burma-Thailand-Laos) and the Golden Crescent (Iran-Afghanistan-Pakistan) has been particularly severely affected.

The most important dependence producing derivatives are morphine and heroin. They both like majority of dependence producing opioids bind to μ (mu) opioid receptors. The other opioid receptors are k (kappa, e.g. for pentazocine), δ (delta, e.g. for a type of enkephalin), σ (sigma, e.g. forphencyclidine), ϵ (epsilon) and λ (lambda). Heroin or di-acetylmorphine is about two times more potent than morphine in injectable form. Apart from the parenteral mode of administration, heroin can also be smoked or 'chased' (chasing the dragon), often in an impure form (called 'smack' or 'brown sugar' in India). Heroin is more addicting than morphine and can cause dependence even after a short period of exposure. Tolerance to heroin occurs rapidly and can be increased to up to more than 100 times the first dose needed to produce an effect.

Acute Intoxication

Intoxication is characterised by apathy, bradycardia, hypotension, respiratory depression, sub normal core body temperature, and pin-point pupils. Later, delayed reflexes, thready pulse and coma may occur in case of a large overdose. In severe intoxication, mydriasis may occur due to hypoxia.

Withdrawal Syndrome

The onset of withdrawal symptoms occurs typically within 12-24 hours, peaks within 24-72 hours, and symptoms usually subside within 7-10 days of the last dose of opioid. The characteristic symptoms include lacrimation, rhinorrhoea, pupillary dilation, sweating, diarrhoea, yawning, tachycardia, mild hyper tension, insomnia, raised body temperature, muscle cramps, generalised bodyache, severe anxiety, piloerection, nausea, vomiting and anorexia.

There are marked individual differences in presentation of withdrawal symptoms. Heroin withdrawal syndrome is far more severe than the withdrawal syndrome seen with morphine.

Complications

The important complications of chronic opioid use may include one or more of the following:

- 1. Complications due to illicit drug (contaminants):Parkinsonism, degeneration of globuspallidus, peripheral neuropathy, amblyopia, transverse myelitis.
- 2. Complications due to intravenous use: AIDS, skin infection(s), thrombophlebitis, pulmonary embolism, septicaemia, viral hepatitis, tetanus, endocarditis.
- 3. Drug peddling and involvement in criminal activities (social complication).

Treatment

Before treatment, a correct diagnosis must be made on the basis of history, examination (pin-point pupils during intoxication or withdrawal symptoms) and/or laboratory tests. These tests are:

- 1. Naloxone challenge test(to precipitate withdrawal symptoms).
- 2. Urinary opioids testing: With radioimmunoassay (RIA), free radical assay technique (FRAT), thin layer chromatography (TLC), gas-liquid chromatography (GLC), high pressure liquid chromatography (HPLC) or enzyme-multiplied immunoassay technique (EMIT).

The treatment can be divided into three main types:

- 1. Treatment of overdose.
- 2. Detoxification.
- 3. Maintenance therapy.

Treatment of Opioid Overdose

An overdose of opioid can be treated with narcotic antagonists(such as naloxone, naltrexone). Usually an intravenous injection of 2 mg naloxone, followed by a repeat injection in 5-10 minutes, can cause reversal of overdose. But as naloxone has a short half-life repeated doses may be needed every 1-2 hours. This should be combined with general care and supportive treatment.

Detoxification

This is a mode of treatment in which the dependent person is 'taken off' opioids. This is usually done abruptly, followed by management of emergent withdrawal symptoms. It is highly recommended that detoxification is conducted in a safe manner under expert guidance of a specialist.

The withdrawal symptoms can be managed by one of the following methods:

1. Use of substitution drugs such as methadone (not available in India at present) to ameliorate the withdrawal symptoms.

The aim is to gradually taper off the patient from methadone (which is less addicting, has a longer half-life, decreases possible criminal behaviour, and has a much milder withdrawal syndrome). However, relapses are common and its opponents argue that one type of dependence is often replaced by another (methadone).

Detoxification

- 2.Clonidineis an α agonist that acts by inhibiting norepinephrine release at presynaptic α receptors. The usual dose is 0.3-1.2 mg/day, and drug is tapered off in 10-14 days. It can be started after stoppage of either the opioid itself or the substitution drug (methadone). The important side effects of clonidine are excessive sedation and postural hypotension. Clonidine treatment is usually started in an inpatient psychiatric or specialist alcohol and drug treatment centre setting.
- 3. Naltrexone with Clonidine: Naltrexone is an orally available narcotic antagonist which, when given to an opioid dependent individual, causes withdrawal symptoms. These symptoms are managed with the addition of clonidine for 10-14 days after which clonidine is withdrawn and the patient is continued on naltrexone alone.
- 4.Other Drugs: The other detoxification agents include LAAM (levo-alpha-acetyl-methadol), propoxyphene, diphenoxylate, buprenorphine (long acting synthetic partial μ -agonist which can be administered sublingually), and lofexidine (agonist, similar to clonidine). In particular, Buprenorphine has recently been used widely for detoxification as well as for maintenance treatment in many parts of the World. Care must be exercised as there is potential for misuse with buprenorphine.

Maintenance Therapy

After the detoxification phase is over, the patient is maintained on one of the following regimens:

1. Methadone maintenance

(Agonist substitution therapy) This a very popular method used widely in the Western World. 20-50 mg/day of methadone is given to the patients to 'shift' them from 'hard' drugs, thus decreasing IV use and criminal behaviour. Its use in India has not been recommended by an expert committee for de- addiction services. Other drugs such as LAAM and buprenorphine can be used for maintenance treatment.

2. Opioid antagonists

Opioid antagonists have been in use for a long time, but they were either partial antagonists (such as nalorphine) or had to be administered parenterally (such as naloxone). Naltrexone combined with clonidine, as described above, is a very effective method for detoxification as well as for maintenance treatment.

Maintenance Therapy

3.Other methods

These include individual psychotherapy, behaviour therapy, interpersonal therapy, cognitive behaviour therapy (CBT), motivational enhancement therapy, self-control strategies, psychotropic drugs for associated psycho pathology, family therapy, and group therapy (e.g. in therapeutic communities such as Synanon, self-help groups such as Narcotic Anonymous or NA). These methods have to be tailored for use in an individual patient.

4. Psychosocial rehabilitation

This is a very important step in the post-detoxification phase, in the absence of which relapse rates can be very high. Rehabilitation should be at both occupational and social levels.