HyperTox© 2004

The advice in HyperTox is not a substitute for good clinical assessment and consultation (v0213)

Home Drugs by class Drugs by name Chemicals Animals/Plants

OPIOIDS

DRUGS INCLUDED IN THIS CATEGORY

- Morphine
- Codeine
- Heroin

- Pethidine (meperidine)
- Diphenoxylate
- Fentanyl
- Methadone
- Oxycodone
- Pentazocine
- (Dextro)propoxyphene

OVERVIEW

Opioids present with a syndrome which includes miosis, coma, respiratory depression and vomiting. A rapid response to naloxone is usual if hypoxic brain damage or other events have not been superimposed. The treatment is primarily supportive, although naloxone may also be used in certain circumstances. In recreational overdoses (i.e. dependent patients), a withdrawal reaction to naloxone is common.

MECHANISM OF TOXIC EFFECTS

Opioids are opioid receptor agonists. Stimulation of these receptors in the central nervous systems leads to analgesia, vomiting and profound sedation in a dose dependent manner. These effects are potentiated by other sedative drugs (e.g. alcohol, benzodiazepines) and the majority of fatal overdoses involve other substances. Non-cardiogenic pulmonary oedema occurs in a substantial number of opioid overdoses, however the mechanism behind this is unknown. Dextropropoxyphene and its metabolite norpropoxyphene have 'antiarrhythmic' (and consequently proarrhythmic) activity. This may lead to arrhythmias and negative inotropic effects. Pethidine and pentazocine have serotonergic effects in addition to their opioid effects and, usually in combination with other drugs, may cause the serotonin syndrome.

KINETICS IN OVERDOSE

The opioids are a diverse group of substances. The most important kinetic difference between them is their half-life in overdose which varies from hours to days.

Absorption

Opioids are generally rapidly absorbed, with peak concentrations within two hours of oral ingestion, one hour of IM administration and minutes of IV injection. First pass metabolism is noted with some of these drugs (codeine, morphine, propoxyphene) however these drugs also have active metabolites. Oral controlled release formulations of morphine and oxycodone and topical preparations of fentanyl are also available and are frequently used in palliative care. Absorption from these preparations will continue for up to 12 hours.

Distribution

These drugs have volumes of distribution of 1-5 L/kg and cross well into the central nervous system.

Metabolism - Elimination

These drugs are primarily hepatically metabolised. The half-life of most of these drugs is between 1 and 5 hours. However methadone (about 24 hours) and propoxyphene (12 to 24 hours) are exceptions.

CLINICAL EFFECTS

Central nervous system effects

CNS depression is the major clinical manifestation. Increasing doses lead to increasing degrees of sedation with initial analgesia and sedation, followed by loss of response to verbal stimuli, loss of response to tactile stimuli, loss of control over normal respiration and failure of temperature and blood pressure regulation.

Cardiac effects

Dextropropoxyphene may lead to cardiac effects and ECG changes. The ECG changes seen in propoxyphene overdose are similar to those seen in tricyclic antidepressant poisoning with QRS and QT prolongation, varying degrees of heart block and tachyarrhythmias.

Pulmonary effects

Aspiration and non-cardiogenic pulmonary oedema are common complications.

Other effects

Pentazocine and pethidine may contribute to the development of a serotonergic syndrome.

INVESTIGATIONS

Imaging

A chest X-ray should be obtained in severe opioid overdose as aspiration and non-cardiogenic pulmonary oedema are common complications.

ECG

An ECG should be done in overdoses involving propoxyphene.

Blood concentrations

Drug concentrations are not helpful in the management of overdose.

Urine drug screen

Patients with recreational overdoses should have a urine drug screen for drugs of abuse to identify other substances that may have been taken or abused.

Other investigations

Patients with suicidal ingestions who present with an opioid syndrome should have paracetamol, salicylate and electrolytes done to detect coingestion of paracetamol and/or aspirin, as combination tablets are a frequent source of codeine or propoxyphene.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis for a patient presenting with a typical opioid syndrome is any other sedating drug. The presence of miosis is not limited to opioid drug overdose but occurs in benzodiazepine, chloral hydrate, barbiturate, phenothiazine, alcohol and organophosphate overdose. A failure to respond to naloxone indicates ingestion (or coingestion) of one of these other drugs is more likely.

DIFFERENCES IN TOXICITY WITHIN THIS DRUG CLASS

Prolonged toxicity is seen with methadone and propoxyphene overdose due to their long half lives and this may necessitate treatment for several days. Propoxyphene may cause direct cardiac effects. Drugs such as codeine, which are prodrugs, have much less toxicity in overdose as they need to be converted to more active metabolites. Drugs administered by the intravenous route in recreational overdoses may involve various adulterants which occasionally will be of clinical importance.

Adulterants found in street drugs include such diverse substances as

- Ketamine
- Quinine
- Talc
- Glucose powder
- Strychnine
- Caffeine
- Other illicit drugs, e.g. amphetamines, barbiturates

Unexplained symptoms in patients with recreational overdose should prompt a search for these substances and should include an ECG to detect cardiotoxic drugs.

TREATMENT

Supportive

Patients should be closely observed for the development of respiratory depression. If necessary, naloxone can be given to counteract the sedating effect of opioids. Intubation and ventilation will occasionally be required for patients who have developed respiratory complications of their overdose.

GI Decontamination

Activated charcoal may be given to patients who have oral ingestions of opioid drugs within 1-2 hours. Controlled release preparations should be treated with activated charcoal and whole bowel irrigation.

Antidotes

Naloxone

Mechanism

Naloxone is a receptor antagonist with a short half life. The duration of action of a single dose is usually less than 1-2 hours. As this is shorter than the duration of action of most opioids, repeat doses are often required to maintain consciousness.

Dose

Naloxone is given 0.4 mg IV or IM repeated up to a total dose of 2 mg. Failure to respond to 2 mg means further doses are unlikely to be helpful. Use the minimum dose necessary to raise the patient's level of consciousness to a point where respiratory depression is avoided and the patient may be woken. Too large a dose of naloxone may not only precipitate opioid withdrawal, but may lead to the patient absconding from the hospital department. As the naloxone wears off over the next hour the patient may then collapse in the gutter outside the hospital (see Coroner/Medical Examiner).

Monitoring and infusions

Patients should be observed carefully for relapse for at least 2-3 hours. If a patient does redevelop marked sedation after their first naloxone dose, an infusion of naloxone may be required (commencing with a dose that is half to two thirds of the dose required initially to wake them given per hour). pCO_2 estimation is the most accurate way to assess respiratory depression due to opioids and should be regularly estimated in patients on infusions.

Controlled release morphine and oxycodone, methadone and propoxyphene overdoses may require a continuous infusion for as long as several days.

Adverse effects

Adverse effects from naloxone are limited to the occasional precipitation of a withdrawal syndrome in patients with chronic dependence.

Treatment of specific complications

Propoxyphene induced arrhythmias

Patients ingesting propoxyphene with abnormal ECGs (increased PR, QRS & QT durations) should be monitored until the ECG returns to normal. Treatment of tachy- and bradyarrhythmias should be similar to that used in TCA poisoning with alkalinisation as the first line therapy.

LATE COMPLICATIONS, PROGNOSIS - FOLLOW UP

Patients with recreational overdoses should be referred to drug and alcohol services. If the patient is not sedated and has not received naloxone within the previous three hours, the patient may be discharged. Patients with propoxyphene overdoses should have ECG monitoring until their ECG returns to normal. Long term sequelae are only likely if there has been a period of hypoxia with subsequent hypoxic brain injury.

REFERENCES - FURTHER READING

Meredith TJ, Jacobsen D, Haines JA, Berger J-C (eds). Naloxone, flumazenil and dantrolene

as antidotes. IPCS/CEC evaluation of antidotes series Vol 1. Cambridge University Press 1993

Chamberlain JM, Klein BL. A comprehensive review of naloxone for the emergency physician. American Journal of Emergency Medicine 1994;12:650-660.

Hoffman RS, Goldfrank LR. The poisoned patient with altered consciousness. Controversies in the use of a 'coma cocktail'. JAMA 1995;274:562-569.

23/12/99 7:33:26. Reviewed IMW 16/6/02

Back to top