Opiate Poisoning

Opiate poisoning can occur at any time from birth (when pethidine given to the mother in labour may suppress ventilation) to terminal care. The outcome can range from minor adverse effects such as constipation to death from respiratory depression. The following drugs may be involved:

- Codeine
- Diamorphine
- Dihydrocodeine
- Fentanyl
- Heroin
- Loperamide
- Meptazinol
- Methadone
- Morphine
- Opium
- Oxycodone
- Pentazocine
- Tramadol

They may come alone or in combination when the situation becomes more complex.

Epidemiology

It is difficult to get reliable incidence figures. The elderly are more liable to poisoning from opiates and more likely to be taking them, especially drugs like co-codamol for arthritis.

The Office for National Statistics (ONS) published figures for deaths related to drug poisoning in England and Wales for the year 2012. During this period there were 579 deaths involving heroin/morphine (a slight fall from the previous year).

The heroin/morphine-related mortality rate for males has reduced significantly in recent years, from 27.7 deaths per million population in 2009 to 15.6 in 2012. This is a 44% fall and the lowest rate since 1997. The fall is thought to be due in part to the heroin ‘drought’ of 2010/2011 with reduced availability persisting subsequently. The corresponding female rate increased slightly between 2011 to 2012 from 4.4 to 5.2 deaths per million population but was still much lower than the corresponding rate in males.

There were 414 deaths involving methadone in 2012, representing a 16% decrease since 2011 in males and a 9% decrease in females. Nevertheless, the female mortality rate remains the second highest on record.

An Australian study of fatal methadone and heroin toxicity cases found that methadone users were significantly more likely than heroin users to have cardiac, pulmonary, hepatic and renal disease.

A rise in drug-related deaths in Scotland was seen in 2006; this was thought to be a late effect of the increase in the use of injectable drugs in the 1980s. However, recent reports show a significant decline in deaths involving heroin or morphine (73% in 2009 to 48% in 2012). The percentage of deaths with methadone present fell to 50% in 2012 from 57% in 2011.

Heroin and morphine remain the most common cause of drug-related deaths, closely followed by methadone. However, there has been an increasing number of deaths involving tramadol (175 deaths in 2012 compared with 83 in 2008).

Polydrug use which was a significant factor in previous years, appears to have reduced significantly in England and Wales. However, it still remains an issue in Scotland.

Risk factors

- Studies of the psychosocial background of drug abusers who died from opiate poisoning show a strong correlation between mental health conditions, financial problems and crime. Being in a relationship tends to have a protective effect.
- A significant incidence in recently released prisoners has been identified. This has been found to be associated with extreme social disadvantage, multiple drug use and risky drug-use patterns.
- One study at the Edinburgh Royal Infirmary found that a high proportion of drug-related deaths occurred in people who had used the hospital in the previous five years.
- Opiates produce tachyphylaxis. This means that, with time, larger and larger doses are needed to obtain the same effect and tolerance develops to the adverse effects. It is not uncommon to find a drug abuser or a patient in terminal care who is taking a daily dose that would be fatal to a normal person. If dosage is reduced or stopped this tolerance quickly fades. If they take what was formerly ‘a good hit’ it has become a fatal overdose.
- Alcohol and other sedatives enhance the effect of opiates, especially respiratory depression. Drug abusers often like to enhance the effect of heroin with benzodiazepines. This is very dangerous.
The following groups are at risk of morphine toxicity and usually require a lower dose:[9]

- Hepatic impairment may produce coma but many such patients tolerate morphine well.
- Reduce dose or avoid in renal impairment, the elderly and the debilitated.
- Hypotension.
- Hypothyroidism.
- Asthma (avoid during an attack) and decreased respiratory reserve.
- Prostatic hypertrophy.

Opiates should still be used in terminal care, even in these groups. Since the Harold Shipman case some doctors are wary about the dose they give, even in terminal care. If this means that dying patients are denied adequate analgesia, it is to be regretted. Morphine or diamorphine can safely be titrated upwards by 30-50% at a time.[10]

Presentation[9, 11]

Symptoms

- Opiate poisoning may be a chronic problem, in which case the main complaint will be of constipation. There may be nausea, vomiting or just loss of appetite. There may be sedation and craving for the next dose.
- Acute toxicity presents with drowsiness that will be more severe if there is also alcohol involved, or involvement of other sedatives. There may be nausea or vomiting.

Signs

- Respiratory depression may be apparent. Hypotension and tachycardia are possible. There are usually pinpoint pupils but this sign may be absent if other drugs are involved.
- The 'post-mortem sole incision' sign has been identified. This is an incision made in the sole by an acquaintance in the belief that the subsequent blood loss will reduce the likelihood of death in an individual who has taken an accidental overdose of an opiate.[12]

Differential diagnosis

There may be no clear indication of what the patient has taken. He or she may be a known drug abuser or there may be needle track marks on the limbs. Beware of multiple drug ingestion (eg, antidepressants, alcohol or benzodiazepines), especially in drug abusers or with suicidal intent.[10]

Other conditions which may need to be considered include:

- Diabetic ketoacidosis.
- Hypercalcaemia.
- Hypernatraemia.
- Hyperosmolar hyperglycaemic nonketotic coma.
- Hypoglycaemia.
- Hypokalaemia.
- Hypothermia.
- Meningitis.
- Stroke.
- Subdural haematoma.
- Syncope.

Investigations

- It is possible to obtain a urine screen for drugs of abuse and there are even some sticks available that will give a quick result. However, they merely detect the presence of opiates or methadone and give no indication of quantity.[13]
- A paracetamol blood level should be considered for all patients who have overdosed or self-poisoned.[14]
- If in doubt, give a small test dose of naloxone, repeating with gradually increasing doses every 2-3 minutes if no response. The following schedule has been suggested for adults:[14]
  - 0.04 mg
  - 0.5 mg
  - 2 mg
  - 4 mg
  - 10 mg
  - 15 mg

- Baseline pathology investigations should be performed in patients with moderate-to-severe toxicity, including FBC, metabolic screen, creatine kinase level and arterial blood gases.[15, 16]
- A CXR may be indicated if pulmonary oedema is suspected.[16]
- Abdominal X-ray has a poor pick-up rate in people suspected of ingesting drug packages and a combination of X-ray and CT scan is advisable.[17]
- ECG should, as a general rule, be considered in all patients.[18]
Associated diseases\textsuperscript{[19]}

Drug abusers may possibly carry hepatitis B (prevalence 5-10% in the UK). Intravenous abusers have a 60-80% chance of carrying hepatitis C. There may possibly be HIV infection. Nutrition and self-care are usually poor.

Management

- Do not delay establishing a clear airway, adequate ventilation and oxygenation if consciousness is impaired.\textsuperscript{[20]}
Give intravenous (IV) (0.4-2 mg for an adult and 0.01 mg/kg body weight for children) if coma or respiratory depression is present.\textsuperscript{[21]}

- Give intramuscularly (IM) if no vein is available. Repeat the dose if there is no response within two minutes.
- Naloxone is a competitive antagonist and large doses (4 mg) may be required in a severely poisoned patient.
- Failure of a definite opiate overdose to respond to large doses of naloxone suggests that another central nervous system (CNS) depressant, or brain damage, is present.
- Observe the patient carefully for recurrence of CNS and respiratory depression. The plasma half-life of naloxone is shorter than that of all opioid analgesics. Repeated doses may be required. Naloxone IM should be considered if the patient is threatening to self-discharge, as it may help reduce the risk of respiratory arrest when the IV naloxone wears off.
- If someone takes an overdose of IV heroin it is important to administer naloxone as soon as possible. Often this is done by paramedics but some people have advocated that users should have a supply in case one of their number overdoses and treatment can be started without delay.\textsuperscript{[22]} They are often reluctant to call for help.
Further reading & references

- IV infusions of naloxone may be useful where repeated doses are required. Naloxone 400 micrograms/ml is diluted with sodium chloride 0.9 % or glucose 5%. Five ampoules of naloxone 400 micrograms/ml (2 mg) per 500 ml give 4 μg/ml. Two-thirds of the bolus dose needed to reverse intoxication given hourly as a continuous infusion often maintains respiratory effort without promoting opiate withdrawal. Infusions are not a substitute for frequent review of the patient's clinical state.

- Give oral activated charcoal, provided the airway can be protected, if a substantial amount has been ingested within two hours.[20]

- Naltrexone is recommended by the National Institute for Health and Care Excellence (NICE) as a treatment option for people who have opioid-dependent but who have stopped using opioids and who are highly motivated to stay free from the drugs in an abstinence programme.[23] It is a competitive opiate antagonist that will block the effect of heroin. It should only be given to people who have been told about the problems associated with treatment and with proper supervision. Treatment with naltrexone should be given as part of a support programme to help the person manage their opioid dependence.

- There is no consensus about the management of patients if body packing of opioids is confirmed. Options include watchful waiting, with or without the use of laxatives, whole bowel irrigation, endoscopic removal or surgery. A risk-benefit analysis should be performed, taking into consideration whether the patient is symptomatic or asymptomatic and whether the treatment is likely to increase or decrease the risk of package rupture. Most patients can be managed by watchful waiting and discharged from hospital as soon as the package has been evacuated with a normal bowel movement.[24] Surgery should only be performed in body packers with signs of intoxication or ileus.[25]

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Prognosis

The development of noncardiogenic pulmonary oedema (also known as acute lung injury) carries a poor prognosis (it is not naloxone-reversible). Multiple drug ingestion and comorbidity (eg, cardiac or renal conditions) also increase the risk of death.[26]

Prevention[27]

Drug abusers must be educated about the risks they face. They must understand loss of tolerance after reduction therapy or enforced abstinence as in prison. They must understand the enhanced risk with benzodiazepine use too. They are much less likely to have a serious overdose if they inhale rather than inject.

Daily dispensing of methadone with supervised consumption has greatly reduced the risks.[28]

Take-home naloxone schemes are effective but pragmatic difficulties such as ensuring adequate supplies may need to be overcome.[29]

Further reading & references

- Palliative care for adults: strong opioids for pain relief; NICE Clinical Guideline (May 2012)
- Reducing drug-related deaths; National Treatment Agency, 2004

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11. Opioids; International Program on Chemical Safety (INCHEM), 2008


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23. Naltrexone for the management of opioid dependence; NICE Technology Appraisal Guidance, January 2007


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