drug isdd link
PHOTOCOPIABLE FACTSHEET

21 Drug Interactions

When a person takes a drug not only does the drug affect them, but *they* affect the drug. The duration of a drug's effect, its 'pharmacodynamics', is related to changes in its concentration in the body over time, its 'pharmacokinetics'. This concentration can be heavily influenced by the individual themselves, not least through the presence of other substances in their bloodstream.

Such 'drug interactions' can either increase or decrease a drug's expected effects. In some cases they are planned – many treatment regimes rely on such interactions, while problematic drug users may actively seek out interactions to 'boost' a drug's effects. But in many other cases, such interactions are not planned, and any adverse consequences can range from the reversible and trivial to the permanent and life-threatening.

Such an interaction may be predictable, occuring every time the particular drugs are combined, or it may be erratic, happening only in isolated cases. Knowledge about interactions is vital in the treatment field, especially is someone is taking medication (anti-epileptics, anti-asthmatics, drugs for heart disease, oral contraceptives, anti-HIV drugs) on top of illegal or legal drugs. Not all interactions are clinically relevant (particularly if the doses are low and are unlikely to be repeated), but this factsheet will highlight a number of the most common interactions between illicit and licit substances.

Amphetamine

Substances that acidify the urine (such as cranberry juice) or alkalinise it (bicarbonate and other over-the-counter indigestion remedies) may have an effect on amphetamine pharmacokinetics. This is because the elimination of amphetamine from the body is increased when urine is acidic and decreased when alkaline. This procedure has been used to reduce the likelihood of amphetamine detection by urine analysis.

LSD+antidepressants

The onset or worsening of LSD 'flashbacks' has been reported among adolescents when they receive antidepressant therapy using a selective serotonin reuptake inhibitor antidepressant (paroxetine – Seroxat).

Chronic use of tricylic antidepressant drugs has been reported to enhance the subjective physical, hallucinatory and psychological responses to LSD.

Cannabis+alcohol

An important interaction is that between alcohol and cannabis – the two most frequently used drugs, besides tobacco. In a study of 14 men and women, the drug combination was found to produce a greater level of impairment than either drug alone.[1] However, little evidence was found that moderate doses of alcohol and cannabis consumed either alone or in combination, produced behavioural or subjective impairment the following day.

Cocaine+alcohol

The interaction between cocaine and ethanol (alcohol) is almost unique. These drugs combine to form a new compound, cocaethylene. This compound arises only when the two drugs are used together. Although cocaethylene is eliminated from the body more slowly than either ethanol or cocaine, its importance remains unclear.

1. Chait L. & Perry J. "Acute and residual effects of alcohol and marijuana, alone and in combination, on mood and performance." *Psychopharmacology*: 1994, 115(3), p.340-9.

HIV/AIDS drugs

The drugs used in the treatment of HIV/AIDS pose particular problems, because many of the currently used antibiotics and antiviral agents have profound effects on the liver enzyme systems, on kidney function and on bone marrow. This can result in changes in the time taken to eliminate other drugs.

Volatile Substance Abuse

Sudden cardiac deaths associated with VSA are thought to result from the action of adrenaline produced in the body acting on a heart sensitised by the presence of high concentrations of the volatile compound. It could therefore be dangerous to administer adrenaline as part of the emergency resuscitation procedure as the same interaction might occur.

Workers occupationally exposed to trichloroethylene – a degreasing agent used in many industries and previously used in correcting fluids – who then drink alcohol can experience transient facial reddening, an uncomfortable condition similar to 'hot flushes' and known as Degreaser's Flush.

Opioid analgesics (morphine, pethidine & methadone)

Many – if not most – drug interactions stem from a drug's effects on the liver enzymes which are largely responsible for the elimination of drugs from the body. These interactions can either slow down or speed up that elimination, and can be most noticeable among the opioid drugs.

An example of the former is the sometimes fatal interaction between pethidine and monoamine oxidase inhibitor antidepressants, an interaction which can cause an extreme increase in body temperature and seizures. An example of an interaction which speeds up a drug's elimination from the body are the withdrawal symptoms which have been reported in patients maintained on methadone when they are given phenytoin or rifampicin.

Another possible reason for interactions involving opioids could be that morphine and pethidine in particular reduce 'gastro-intestinal motility' (the process by which food is moved through the gut). This in turn could decrease the rate of absorption of other drugs which have been taken by mouth. On the other hand, metoclopramide, a drug given to prevent nausea, has been reported to increase gastro-intestinal motility and therefore speed up the onset and sedative effects of orally administered morphine.

Antibiotics are often used with opioids in patients undergoing medical or surgical procedures. The best documented metabolic interactions are with erythromycin and rifampicin. Erythromycin increases and rifampicin decreases the effects of opioids. Some of the drugs used to treat epilepsy, particularly carbamazepine, phenytoin and barbiturates, can speed up the metabolism of opioids in the liver.

The tricyclic antidepressants, clomipramine and amitriptyline, significantly increase the plasma availability of morphine when given to cancer patients taking oral morphine solution. There are isolated reports of interactions between histamine H(2) antagonists (drugs like cimetadine and ranitidine used to treat ulcers) and opioids. The effects include breathing difficulties, confusion and muscle twitching.

One of the most dramatic examples of a drug interaction is that used in the 'rapid opiate detoxification' regime, when a small dose of naloxone (0.5 mg) is injected into opioid dependent people. This is likely to precipitate a withdrawal syndrome very similar to that seen after the abrupt withdrawal of opioids, except that the syndrome appears within minutes and subsides in about two hours.