Fentanyl (1-phenethyl-4-N-propionylanilinopiperidine) is a potent but short-acting opioid receptor antagonist. It is estimated to be up to 75-100 times stronger than morphine but mainly affects µ-opioid receptors in the central nervous system. Medically, it is used for analgesia and anaesthesia.

Fentanyl is used illicitly for its euphoric and sedative effects although the euphoric effect is considered to be milder than with morphine. Tolerance and physical addiction to fentanyl can develop quickly through persistent use. Fentanyl toxicity is mediated through opioid receptors. Typical signs of fentanyl poisoning include respiratory arrest, central nervous system depression (coma), muscle rigidity and miosis (pinpoint pupils). Other symptoms include bradycardia or decreased heart rate, hypotension and bowel obstruction. Urine output is also reduced. Withdrawal symptoms are typical of opiates and include myalgia (muscle pains), flu-like symptoms, tremors, anxiety, agitation and nausea but can be exceptionally pronounced.

Risks of recreational fentanyl use

Fentanyl is a highly potent drug and, as such, carries a serious risk of overdose. Respiratory arrest can develop rapidly. The non-clinical use of fentanyl patches, including sucking, swallowing, extraction and intravenous use, (Durogesic®, Matrifén®, Fentanyl® [several manufacturers]) represents a particularly high risk. There is no way of controlling the dosage when administered in this manner but the effects may take place very rapidly, which can prove fatal. The strongest patches worn on the skin may be extremely dangerous for opiate-naive users, especially if they are “left” on during sleep. Changes to the skin, including the effects of temperature change on blood flow, may accelerate absorption by up to a third, leading to toxicity. Used and discarded patches are also dangerous as, due to their design, they still contain high levels of fentanyl.

Recreational users who cut smaller pieces out of patches may misjudge the dosage by assuming that the size of the piece they are cutting is directly proportional to the amount of fentanyl it contains. Although the size may give some indication of the likely concentration, this practice is by no means recommended. When the patches are cut, the depot structure is broken, which can result in an uncontrolled release of fentanyl. The exact make up of the patches can vary between manufacturers and the sizing has not been standardised. There have been attempts to improve the safety of the patches, including distributing the fentanyl evenly throughout a matrix rather than storing it in a reservoir.

Concomitant use with other CNS medications, including benzodiazepines, alcohol or other opiates, increases the risk of overdose. As fentanyl is metabolised mainly by the CYP3A4 liver enzyme, the administration of other therapeutic agents or other substances may in some cases lead to marked changes to fentanyl concentrations in the body. In addition to patches, fentanyl is also available as a spray and as oral and parenteral formulations.

Dosage

When fentanyl is administered subcutaneously or intravenously, 1mg of morphine is estimated to equate to 0.01mg (or 10mcg) of fentanyl. The oral transmucosal administration of fentanyl is estimated to be 40 to 70% more effective than IV administration. If a patch contains “25mcg/h” of fentanyl, it means that 25 micrograms of fentanyl is released per hour. Usually, a patch is worn for a period of 72 hours, meaning that the total dose over that period of time is 25mcg/h x 72 = 1800mcg or 1.8mg. This dose is 18 times greater than the 100mcg used intravenously to induce general anaesthesia when full resuscitation facilities are available. The strongest patches (100mcg/h) contain up to 72 times this dose. A lethal dose is currently estimated at 2mg but individual susceptibility varies greatly.

When fentanyl is administered intravenously, the effect is immediate and peaks within a matter of minutes. When used for analgesia, the effects are estimated to last for 30 to 60 minutes. Increasing the dose to lengthen the effect can often lead to the administration of a lethal dose, which is why fentanyl in the healthcare setting is commonly administered as a continuous infusion or intermittent bolus doses or via a depot patch. The patches take effect over a period of several hours, with a steady concentration achieved within 12 to 24 hours. The onset of any side effects will also be delayed.

Fentanyl-related death
Respiratory depression or breathlessness is an alarming sign of an impending fentanyl overdose. An overdose can be treated with an opioid antagonist such as naloxone but treatment must commence promptly. It appears that some fentanyl users have a buprenorphine syringe available in case of an overdose. Buprenorphine is a partial antagonist and there is currently no scientific evidence of its effectiveness as a first-line treatment for fentanyl overdose. Naloxone should therefore be considered the only available antidote. Since 2006, fentanyl has been associated with more than 30 deaths in Finland. In many of the cases, there has been evidence of concomitant recreational drug use but in some of the cases users have simply not been fully aware of the dangers posed by fentanyl.

If you suspect that you or someone else is suffering from a fentanyl overdose, dial 112 immediately or contact the Poison Information Centre at 09 471 977. CPR must be commenced immediately and it must be continued until paramedic or other healthcare staff arrive.

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References


Pharmaca Fennica 2010.


link

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