Smoking fentanyl can cause irreversible brain damage, report shows

May 21 2024, by Colin Davidson

Credit: Anna Shvets from Pexels
A middle-aged American man with no previous medical history was found unconscious in his hotel room, with "unidentified crushed pills and a white residue" on a nearby table, according to a recent paper in *BMJ Case Reports*. White powder was visible around the man's mouth.

This situation would be fairly unremarkable for a country that is in its tenth year of an illicit fentanyl epidemic. However, there was something remarkable about this case. It was the first reported instance of toxic leukoencephalopathy—damage to the brain's white matter from a toxic substance—from smoking fentanyl.

There have been many previously reported cases of toxic leukoencephalopathy, or TLE, in people who smoke heroin (known as "chasing the dragon"). Unfortunately, it can also be caused by immunosuppressant drugs and chemotherapy.

In a 15-year review of 101 patients in an American hospital with TLE, the largest group (35) had had chemotherapy, 19 had taken opiates and 11 had been on immunosuppressant drugs.

There have also been previous reports of fentanyl causing TLE. These include TLE from fentanyl patches, from people accidentally swallowing fentanyl patches and from people taking fentanyl pills.

**The damage done**

In the study presented, the 47-year-old man had obvious damage to two brain structures: the cerebellum and the globus pallidus. The cerebellum is involved in, among other things, movement and coordination. The globus pallidus is also important for movement, and it is one of the few areas targeted with deep brain stimulation (a kind of pacemaker for the
brain) for treating Parkinson's disease.

Other drugs cause brain damage (TLE) in other brain areas, such as the hippocampus (important in memory) and the thalamus (a sensory relay station). However, there is not enough data to determine if certain drugs cause TLE in certain brain areas.

The symptoms of TLE range from mild confusion to coma and death. This man was unresponsive when found and required considerable hospital treatment.

He was hospitalized for 26 days before being transferred to a specialist nursing facility for another month after which he was sent home. He received further physiotherapy, occupational therapy and psychotherapy as an outpatient and returned to work, having made a full recovery, within a year. The patient has no memory of the episode.

Other patients with TLE have been less lucky. In a review of 51 cases of substance-abuse-related TLE, 40% of the patients had died within one month. Only four patients made a full recovery.

Given that people who inject heroin and fentanyl can also develop TLE, then the route of drug-taking may be less important than the drug itself. However, as smoking or inhalation of fentanyl or heroin allows the drug to get into the brain faster, and in greater concentrations, then it is reasonable to assume that this may be a more dangerous way to take the drug.

It is likely that more cases of fentanyl TLE will come to light given the drug's increased use in the US and the UK. In addition, it was recently reported that more people in the US now die from smoking illicit drugs than from injecting them.
Although fentanyl is much more potent than heroin and morphine, there are even more powerful synthetic opioids out there. Nitazenes are an emerging illicit class of synthetic opioids that are even more potent drugs than fentanyl and heroin.

Clinical evidence is scarce, but studies in rats show that nitazenes can reduce pain and stop breathing at lower doses than fentanyl. In addition to nitazenes, there are also new synthetic opioids called brorphines that are also very potent.

A conclusion from the new case report from *The BMJ* is that medics should add fentanyl to their routine toxicity screening tests. Given the emergence of nitazenes and brorphine, and their increased potency, it would also be important to develop a screening method to identify these drugs.

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