K33 Postmortem Fentanyl Levels Following Chronic Administration With an Infusion Pump

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The goals of this presentation are to report the levels of fentanyl found in postmortem tissue and fluid samples from a patient chronically administered fentanyl, intravenously (IV), via a patient controlled analgesia (PCA) infusion pump.

Fentanyl is a synthetic narcotic analgesic routinely used as an adjunct in anesthesia or for the management of chronic pain in the form of a transdermal patch (Duragesic®). More recently, clinical studies have shown that fentanyl can be used as an alternative medication in continuous infusion to patients who require high doses or become refractory to traditional opioid treatments. Fentanyl is 50-100 times more potent than morphine and has a short duration of action. Fentanyl is not to be used for acute pain and is given in therapeutic doses of 25-100 micrograms/hr for chronic pain.

A case study is presented to document the postmortem levels of fentanyl found in an individual who had a history of chronic pain. The deceased, a 62 year old female Caucasian, was found dead in bed with an IV line to her subclavian vessel attached to a PCA from which she was being administered fentanyl.

Methods and Results: Fentanyl was extracted from the samples by solid phase extraction with an elution solvent of isopropanol/dichloromethane/ammonium hydroxide (18:80:2). The extracts were analyzed by electron ionization, gas chromatography/mass spectroscopy, operating in the selected ion monitoring mode, utilizing deuterated fentanyl as the internal standard. The following ions were monitored, *245*, 146, 189, *250*, 151, 194, with a calibration curve ranging from 5-100 ng/mL.

The results of the toxicological analyses performed for fentanyl are shown in the table below. The blood was also found to contain therapeutic levels of carisoprodol, meprobamate, fluoxetine, norfluoxetine, nordiazepam, and acetaminophen. In addition, hydrocodone was present at a level of 0.34 mg/L.

Source of Sample	Aorta	Vena Cava	Liver	Vitreous Humor	IV Bag
Fentanyl Conc.	100 ng/mL	95 ng/mL	64 ng/g	5 ng/mL	42,000 ng/mL

The patient had been prescribed fentanyl, administered by continuous infusion, intermittently for two years to treat chronic back pain and pain caused by pancreatitis. The dosing regimen usually began at 60 micrograms/hr and tapered off to 40 micrograms/hr over a few weeks. At the time of death, a dose of 40 micrograms/hr was being administered. The PCA prescription also allowed for a bolus dose to be delivered at a rate of 5 micrograms/6 min, resulting in a maximum dose of 90 micrograms/hr. According to the PCA program, the dose was last adjusted three weeks prior to death. Other drugs detected during toxicological analyses were present at concentrations consistent with the prescribed dosing of the patient.

There is limited information published regarding fentanyl delivered to chronic-pain patients via continuous infusion, IV. A review of the literature shows that fatal overdoses have been reported in the range of 3-139 ng/mL of fentanyl in heart blood, with cases as high as 800 ng/mL. Corresponding liver values are generally 2-7 times higher than the heart blood. However, these results pertain to the Duragesic® transdermal patch or acute dosing of the drug by self-administered intravenous injection or oral ingestion.

The toxicological findings on the blood were high by therapeutic standards although the cause of death was not attributed to an overdose of fentanyl. The patient was not a naïve user of fentanyl, or other opioids, and the corresponding liver and vitreous fentanyl levels were not proportionally as high as the blood. The patient had previously tolerated the current dose of fentanyl, and higher. The patient also had a history of chronic respiratory illness and lupus. It is recommended by the authors that a complete toxicological analysis be performed on all available specimens, and that a comprehensive history be gathered before drawing a conclusion as to the cause of death, especially on the basis of one blood value alone.

To the authors' knowledge, this is the first reported case of postmortem fentanyl concentrations after administration via a continuous infusion pump.

Fentanyl, Infusion Pump, Overdose

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