Reliability of Postmortem Fentanyl Concentrations in Determining the Cause of Death

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Abstract

Introduction Transdermal fentanyl, an opioid used for management of marked pain, also is abused and may cause death.

Methods We reviewed medical examiner reports of 92 decedents who had one or more fentanyl transdermal patches on their body and had fentanyl detected in their postmortem toxicology analysis.

Results The manners of death included 40 accidents, 36 natural, 8 suicides, 5 therapeutic complications, and 3 undetermined deaths. Among the accidental fentanyl intoxication deaths, 32 of 37 involved substance abuse. The majority (95 %) of the 37 accidental deaths involving fentanyl were multi-drug intoxications. The substance abuse deaths had a mean fentanyl blood concentration (26.4 ng/ml or $\mu\text{g/L}$) that was over twice that of the natural group (11.8 ng/ml). Our analysis suggests a relationship between total patch dosage and mean postmortem fentanyl concentration up to the 100- $\mu\text{g/h}$ dose.

Conclusions The very wide and overlapping ranges of postmortem fentanyl concentrations effectively nullify the utility of correlating the dose and expected postmortem concentration for any particular death. Based on the variable relationship between dose and blood concentration, the antemortem dose cannot be reliably predicted based on the postmortem concentration. This does not, however, render the medical examiner/coroner unable to determine the cause and manner of death because the toxicology results are only one datum

point among several that are considered. Although there was a weakly positive relationship between body mass index and fentanyl concentration, further research is needed to determine whether adipose tissue represents a significant depot for postmortem release of fentanyl.

Keywords Toxicology · Fentanyl · Fatality · Forensic pathology · Transdermal · Intoxication

Fentanyl, a synthetic phenylpiperidine, is a prescription opioid that is used for management of marked pain and the induction of anesthesia [1–3]. It has agonist activity at the μ -opioid receptor that results in analgesia and euphoria and is a schedule II medication that has a high potential for abuse. It may be administered by intravenous, transdermal, epidural, transmucosal, and inhalational routes. Due to slow absorption, the transdermal route is prescribed only for treatment of chronic pain. Transdermal (TD) delivery occurs by passive diffusion of fentanyl through the epidermis and dermis into the systemic circulation. Due to fentanyl's lipophilicity, it rapidly diffuses through the epidermis but is delayed by the water-rich dermis. This results in a depot of fentanyl at the epidermis–dermal junction, which explains both the slow onset and prolonged effects of TD fentanyl that may continue even after removal of an unspent patch.

We have reviewed 92 deaths in which the decedent was found to be using one or more fentanyl patches. The causes of death, indication for use, evidence of abuse, postmortem toxicologic results with concentrations, and the epidemiology are examined and discussed. Our goal is to examine the relationship between the fentanyl dose, postmortem concentration, and cause of death. Because of the lipophilicity of fentanyl, we also will examine if postmortem fentanyl concentrations are higher in obese individuals due to increased postmortem release of fentanyl from adipose tissue.

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Materials and Methods

The New York City Office of Chief Medical Examiner (OCME) investigates all unexpected, violent, and suspicious deaths in New York City. By statute, these deaths must be reported to the OCME. From medical examiner death certificates and toxicology records (tracked cases with fentanyl patches reported at autopsy) between January 1, 2003 and August 15, 2011, we identified all decedents who had one or more fentanyl transdermal patches on their bodies and had fentanyl detected in their blood, urine, brain, and/or vitreous fluid. Four decedents with fentanyl patches and no fentanyl detected by toxicologic analysis were not included in the study. City medical examiners investigated, certified, and performed autopsies on all decedents.

The autopsy and death certification data, medicolegal investigation report, toxicology results, and other relevant documents (e.g., hospital reports) in the OCME file were extracted for each case by one of two of the authors (JRG and PTL) using standardized abstraction forms. Discussions occurred to clarify coding rules and ambiguous data. The extracted data was analyzed in a Microsoft Excel spreadsheet with categories that included cause and manner of death, demographics, toxicologic qualitative, and quantitative results by specimen site, place of death, any medical, psychiatric, or substance abuse history, the number and dose of the patches, the location of the patch(s) on the body, length of patch use, estimated postmortem interval, body mass index (BMI), and evidence of decomposition.

The original designation of substance abuse was made by the medical examiner who certified the death. Our review concurred with their designation based on a history of substance abuse and/or the presence of an illicit substance detected by the toxicologic analysis. Prior to autopsy, all deaths were investigated by a medicolegal investigator who went to the scene of death or spoke to the treating physician for deaths pronounced at the hospital. These investigators examined the scene for illicit drugs, drug paraphernalia, and medications. These investigations also included interviews of the next-of-kin or primary care physician to obtain additional medical history and the clinical circumstances. This information is included in the medicolegal investigation report.

Postmortem blood was collected, preserved with sodium fluoride, and stored at 4 °C. There were 35 peripheral, 27 central, 4 cavity, and 26 undesignated blood specimens. Toxicologic analysis was performed on all decedents by the Forensic Toxicology Laboratory at the Office of Chief Medical Examiner. Ethanol concentrations were determined in blood using head space gas chromatography. Specimens were routinely screened for opioids, barbiturates, amphetamines, benzoylecgonine (BE), and benzodiazepines by enzyme or radioimmunoassay. Confirmation and quantitation of morphine, codeine, and benzoylecgonine were

performed using gas chromatography/mass spectrometry (GC/MS). Urine or blood also was analyzed by gas chromatography for basic drugs, including cocaine, phencyclidine, and methadone with confirmation by GC/MS.

A competent cause of death includes the proximate (underlying) cause, defined as that which in a natural and continuous sequence, unbroken by any efficient intervening cause, produces the fatality and without which the end result would not occur. The manner of death is determined from the cause and circumstances of death. The manners of death listed on the United States Standard Certificate of Death include: natural, accident, suicide, homicide, and undetermined. In addition to the standard manners of death, medical examiners in New York City have the option to certify a death as therapeutic complication (TC) [4]. The TC manner of death is used for fatalities due to predictable complications of appropriate medical therapy. In general, acute intoxication deaths (and deaths with acute intoxications as contributing conditions) are chemical injuries and certified as accidents when the death is inadvertent and/or there is evidence of substance abuse. A suicide or homicide manner may be used when evidence supports it [5].

The conclusion that death was caused by an acute intoxication requires that three conditions be met: the toxicology results must be within the range typically encountered in such fatalities, the history and circumstances must be consistent with a fatal intoxication, and the autopsy must fail to disclose a disease or physical injury that has an extent or severity inconsistent with continued life. In deaths caused by drug intoxication with more than one drug in concentrations greater than trace amounts, it is customary to include all of the identified drugs that may play a physiologic role in the cause of death (e.g., acetaminophen would not be included in an acute fentanyl intoxication). The drug concentration is considered to a certain extent when determining the cause and manner of death. Due to a multitude of ante- and postmortem factors, however, the concentration usually is not determinative by itself (see [Discussion](#) below). Some findings, such as a concentration that is an order of magnitude higher than what is typically observed, may favor suicide over accident. Ultimately, the determination of the cause and manner of death in a suspected drug intoxication death is based on a careful review of the entire case including the circumstances, medical history, autopsy findings, and toxicology results.

Data analysis was performed using Microsoft Excel. Linear trend lines for scatter plots were graphed using Microsoft Excel which uses the method of least squares. According to the policies of the New York City Office of Chief Medical Examiner and New York University School of Medicine, this research did not require IRB approval; however, it was submitted to and approved by the OCME legal office.

Results

There were 92 deaths: the age ranged from 13 to 86 years (mean=49.2 years) and the racial/ethnic breakdown included 62 White, 16 Hispanic, and 14 Black. There were 52 males and 40 females. The causes of death are listed in Table 1. The manners of death included 40 accidents, 36 natural, 8 suicides, 5 therapeutic complications, and 3 undetermined deaths. Among those noted to be accidental fentanyl intoxication deaths, 32 of 37 involved substance abuse (the remaining three of 40 accidents were due to blunt trauma (two) and salicylate intoxication (one) and fentanyl did not cause or contribute to these deaths). There were five deaths that had medical reasons for fentanyl administration (e.g., sickle cell disease and chronic pain syndromes) and no known history of substance abuse. These five deaths were due to acute intoxications but it was not clear if the medications were used properly or if there was a component of abuse. If the fentanyl was prescribed for the patient but there was evidence of abuse, the intoxication death is classified as accident. Four of the five therapeutic complication deaths involved fentanyl as the cause or contributing cause of death (one therapeutic complication death was due to a post-operative infection and fentanyl did not cause or contribute to death). For example, one fentanyl intoxication death occurred in an opioid naive woman who received a 50- μ g/h patch for arthritis pain who was found dead the day after applying the first patch. Among those classified as natural death, the reason for the fentanyl prescription was cancer

(18), arthritis (9), and other chronic pain syndromes in the remaining 9 (e.g., sickle cell disease, osteoporosis with compression fractures). Of the 18 decedents with malignancies, 78 % had metastatic disease.

Toxicological analysis was performed for all decedents. The toxicology results are in Table 2. The majority (95 %) of the 37 accidental intoxication deaths involving fentanyl were multi-drug intoxications. The substance abuse intoxication deaths had a mean fentanyl blood concentration (26.4 ng/ml or μ g/L) that was over twice that of the natural group (11.8 ng/ml). Two accidental deaths had fentanyl detected only in the vitreous or urine. In two natural deaths, fentanyl was detected in the blood but could not be quantitated (decomposed remains); they are not included in the summary data in Table 2. Of all the intoxication deaths, there were three sole acute fentanyl deaths of which one involved a decedent with no known history of substance abuse (sickle cell disease patient). The most common co-intoxicants among the 37 accidental intoxication deaths were: benzodiazepines (19), antidepressants (15), cocaine (9), oxycodone (7), morphine/codeine (6), hydrocodone (5), quetiapine (5), and methadone (4). Illicit substances (i.e., cocaine, heroin, or amphetamine) were detected in 12/32 (38 %) of the substance abuse deaths. Among the 36 natural deaths the following co-administered drugs were identified: antidepressants (11), oxycodone (9), benzodiazepines (7), morphine/codeine (5), and hydrocodone (4) (see Table 5).

Table 1 Causes of death

Cause of death	Natural	Accident	Suicide	Therapeutic complication	Undetermined
Acute multidrug intoxication including fentanyl		32	8	1	
Malignancy	18				
Arteriosclerotic cardiovascular disease (ASCVD)	6				
Chronic obstructive pulmonary disease	4				
Acquired immunodeficiency syndrome (AIDS)	2				
Sickle cell disease	2				
Psoriatic arthritis	1				
Epilepsy	1				
Peptic ulcer disease	1				
Neurofibromatosis	1				
Surgical complication ^a				2	
Acute fentanyl intoxication		3		2	1
Blunt Injury		2			
ASCVD with acute intoxication ^b		2			
Acute salicylate intoxication		1			
Undetermined					2
Total	36	40	8	5	3

^aOne was a hemorrhagic complication following a uvuloplasty for sleep apnea and the other was an infectious complication following resection of a spinal malignancy

^bIn two instances, the cause of death was ASCVD with an acute multidrug intoxication including fentanyl as a contributing factor. The intoxication component changes the manner of death from natural to accident

Table 2 Fentanyl toxicology results

Manner	Accidents (Substance Abuse)	Natural	Suicide	Therapeutic complication
Number	31 ^a	34 ^b	8	5
Range, fentanyl concentration, blood (ng/ml)	1–102.2 ^a	1–78	3–462	6.3–14.3
Mean, fentanyl concentration, blood (ng/ml)	26.4 ^a	11.8	95.8	8.7

^a One death with a prolonged hospitalizations was excluded because fentanyl was detected only in the postmortem vitreous sample

^b Two natural deaths were excluded because fentanyl was detected but could not be quantitated

In 35 of the 92 cases, there were multiple patches on the body. Of those with multiple patches, the distribution was: two patches (16 cases); three patches (5 cases); four patches (5 cases); five patches (2 cases); greater than six patches (7 cases). The largest number of patches on a body was 45, which was a suicide. For the suicidal fatalities, the number of patches ranged from one (50 µg/h) to 45 (100 µg/h) patches. All of the suicides were multidrug intoxications. For the accidental deaths, the patches ranged from one (25 µg/h) to nine (12.5 µg/h). For the natural deaths, the patches ranged in number from one (25 µg/h) to three (100 µg/h each) and there was one with four patches but the dose was unknown. The total dosage (number of patches on body multiplied by dosage of the patches) could be calculated in 59 deaths. The total dosage ranged from 25 to 4,350 mcg/h. The total dosage vs. postmortem fentanyl concentration in blood is shown in Fig. 1. There is a general trend towards higher mean postmortem blood fentanyl concentrations with higher total cumulative dosage. Notably, there is a wide range with a measured postmortem fentanyl concentration as low as 2 ng/ml in decedents with a total dosage of up to 300 mcg/h (see Tables 2 and 3). Enough data was available to calculate the body mass index for 86 of the 92 bodies. Of these cases, 15 had a total fentanyl dosage of 100 mcg/h, which was the largest category of fentanyl dosage in our study. A graph depicting the relationship between body mass index and postmortem fentanyl concentration for 100 mcg/h dosages is shown in Fig. 2.

Fig. 1 Patch dosage vs. postmortem concentration

Discussion

Fentanyl intoxication deaths have been reported in two distinct subpopulations of decedents [6–9]. The first is those who administer fentanyl intravenously, often in localized epidemics associated with illicitly produced fentanyl [10–14]. The second group involves deaths due to fentanyl derived from commercially available transdermal patches [15–19]. Although many of these deaths have occurred with dermal use, misuse of patches by the oral, inhalational, or intravenous route are well described [8, 20–24]. In the USA, there has been a substantial increase in prescription opioid abuse and deaths, which includes both oral dosage formulations as well as transdermal patches. This is one of the largest series examining deaths with only transdermal fentanyl administration.

Fentanyl patches currently may be prescribed in five dosage units: 12.5, 25, 50, 75, and 100 µg/h. In the living, the dose administered generally correlates with measured blood concentrations. In the postmortem setting, however, there are several factors that may affect the concentration and should be considered when interpreting postmortem concentrations [7, 25–29]. These include tolerance, post-mortem intervals and redistribution, and metabolism. With regard to transdermal patch use, there are additional factors to consider such as the duration of patch use, body habitus, and site of administration (torso vs. extremity), ambient and body temperature, and whether heating pads or other therapeutic adjuncts were used which potentially may alter the rate of fentanyl absorption. If multiple patches are used, it may not be known whether patches were placed on the body simultaneously or sequentially. Furthermore, the patch may have been defective or tampered with and so fentanyl may be released at a higher or lower rate than intended. For this last reason, it may be prudent in suspected intoxication deaths for the medical examiner to retain the patch in evidence for possible future examination should litigation arise.

Post-mortem redistribution may alter drug concentrations, and may depend on the collection site of the sample. Fentanyl, which has a large volume of distribution, may exhibit postmortem redistribution with heart-femoral blood ratios that ranged from 0.7 to 4.6 (mean 1.6) in 13 deaths with fentanyl transdermal patches [15, 25]. The degree of

Table 3 Mean fentanyl concentrations for various fentanyl patch dosages

Total dose (mcg/h) of all patches	N	Mean fentanyl concentration (ng/ml)	Range	Standard deviation
25	4	2.7	1–5	1.78
50	10	9.18	3–23	6.84
75	3	17.9	10–54	22.30
100>200	22	20.5	1.9–102.2	23.95
200>300	9	27.4	1–69.4	23.31
300>400	7	24.8	2–37	15.33
400>500	2	21.9	21.8–22	0.14
1,900	1	171.0	–	–
4,350	1	462.0	–	–

postmortem change in the peripheral blood similarly has wide variation from pre- to postmortem [25, 30]. Theoretically, prolonged agonal states (e.g., survival for hours with a hypoxic–ischemic encephalopathy) may result in lower postmortem concentrations due to ongoing metabolism prior to death. Since the length of this survival interval may not be known, or if known to be prolonged, a relatively low postmortem concentration should not dismiss intoxication as a possible cause of death if other autopsy finding and circumstances support this conclusion.

Based purely on the blood concentration, these factors may make it difficult to determine whether fentanyl caused the death or is an incidental finding. In 2000, a study in Los Angeles of 25 deaths with transdermal patches concluded that postmortem blood concentrations following therapeutic administration can range up to 7 ng/ml (see Table 4) [15]. The concentrations of the deaths certified as natural ranged from 1.8 to 81 ng/ml while the accidental intoxications ranged from 3.5 to 139 ng/ml. The authors of the Los Angeles study stated that two cases appeared to be misdiagnosed and they did not agree with the cause of death determinations (i.e., decedent with an 81-ng/ml blood concentration had been certified as a natural death due to

heart disease). Although they may be correct, more details would be needed to give an opinion about the cause and manner of death. With the exclusion of the two cases that the authors deemed not natural, the remaining non-fentanyl-related deaths had a mean fentanyl blood concentration of 3.6 ng/ml (range, <2–7 ng/ml). This is much lower than the 11.8 ng/ml that we report in the non-fentanyl-related deaths.

In 2007, a study by Hull et al, examined postmortem fentanyl concentrations for fatalities associated with licit and illicit use (eight). The illicit group had a higher mean fentanyl concentration (17.1 ng/ml) compared to the licit group (4.4 ng/ml). A study in Hennepin County examined postmortem fentanyl concentrations in 23 fatalities [7]. There were eight accidental “drug overdose” deaths in which fentanyl was deemed solely responsible. Of these, the mean blood concentration was 36 ng/ml (range, 5–120 ng/ml). There were four deaths in which fentanyl was an incidental finding (these concentrations were 2, 2, 2, and 15 ng/ml). The decedent with the 15 ng/ml was treated for chronic pain due to metastatic squamous cell carcinoma of the head and neck, suggesting significant tolerance had developed. The dose and route of administration were not described. Other studies have also demonstrated a wide range of fentanyl concentrations (see Table 4).

Our results detected a mean fentanyl blood concentration of 26.4 ng/ml in the intoxication deaths and 11.8 ng/ml in the incidental (non-fentanyl-related) group. As the Hennepin study noted, there may be a considerable overlap in fentanyl concentrations between fentanyl-related intoxication deaths and hospitalized patients treated for chronic pain. These authors concluded that postmortem fentanyl concentrations must be interpreted in the context of the decedent's medical and medication histories and autopsy findings [7]. In some instances, when history is lacking or there are conflicting autopsy findings, the cause and/or manner may be certified as undetermined.

Co-intoxicants are commonly found with both licit and illicit fentanyl use. In 2011, a study by Krinsky et al found among their fentanyl intoxication deaths that 72 % were multidrug intoxications [6]. In our study, 92 % of the accidental intoxication deaths involved the detection of multiple drugs. Among the natural deaths, a similar distribution of sedative and pain medications was also noted (see Table 5). The decision to include other detected drugs in the cause of death statement may depend upon the local customs of the certifier. Since it is often difficult to tease out the role that each substance plays in the death, all intoxicants detected in greater than trace concentrations usually are included. If there is one drug, however, that is substantially more likely to be responsible due to its concentration or inherent toxicity, or if the circumstances may explain certain concentration patterns, the certifier should use their judgment.

Fig. 2 BMI vs. postmortem concentration (100-mcg/h dosages)

Table 4 Summary of fentanyl studies

Reference study	Year	Total decedents	Intoxication, illicit use, mean (<i>n</i> , range) ng/ml	Intoxication, licit use, mean (<i>n</i> , range) ng/ml	Intoxication, mean (<i>n</i> , range) ng/ml	Natural, incidental use, mean (<i>n</i> , range) ng/ml	Patch present
Henderson [12]	1991	112	3.0 ^a (112, 0.2–>800)				0/112
Smialek et al [10]	1994	30			18 (30, 2.2–100)		0/30
Edinboro et al [31]	1997	1		25 (1,25)			1/1
Anderson, et al [15]	2000	25			28 (14, 3.9–139) ^b	28 (5, 1.8–81) ^b	25/25
Kuhlman et al [19]	2003	23	22 (6, 10–36) ^c		12 (11, 2.7–33)		9/23
Martin et al [9]	2006	112	25 (54, 30–383) ^d		36 and 31 (19, 5–152) ^e	5.2 (4, 2–15)	62/112
Thompson et al [7]	2007	23		4.4 (26, trace–17)			7/23
Hull et al [8]	2007	107	17 (55, 0.44–57) ^f		22.8 (350, 0.8 – 164)		6/107
Denton et al [11]	2008	350			40 (1, 40)		0/350
Biedrzycki et al [17]	2009	1			19 (5, 10–28)		1/1
Jumbelic [16]	2010	8		13 (3, 5–22)			8/8
Olson et al [25]	2010	20			4.6 and 17.3 (20, ND–52.5) ^g		14/20
Krinsky et al [6]	2011	96			22.8 (96, 2–400)		58/96
Andresen et al [30]	2012	122				9.1 (118, 1.1–78.6)	118/118

ND not detected

^a Mean excluded six deaths with concentrations greater than 50 ng/ml^b The authors did not agree with the intoxication classification in several deaths and only liver was analyzed for fentanyl in one fatality. There were three suicides and two undetermined deaths^c Three additional decedents had used transdermal and intravenous fentanyl^d Includes transdermal and other routes of administration. The remaining 47 were mixed drug intoxications or other^e Means given for pure fentanyl intoxication deaths (36 ng/ml) and co-intoxicant deaths (31 ng/ml)^f Thirty-eight of 55 deaths were certified as intoxications^g Two samples were collected at different postmortem intervals

Table 5 Other detected substances by manner of death

Other detected substances	Accidental intoxication (n=37)	Natural (n=36)
Opioids		
Oxycodone	7	5
Morphine/codeine	6	9
Propoxyphene	2	3
Methadone	4	4
Hydrocodone	5	4
Hydromorphone	0	2
Heroin	1	0
Sedative/hypnotics		
Benzodiazepines	19	7
Zolpidem	2	1
Stimulants		
Cocaine/BE	9	1
Amphetamine	0	1
Psychotropics		
Amitryptiline/desipramine	8	6
Paroxetine	3	0
Quetiapine	5	1
Citalopram	4	5
Other		
Diphenhydramine	4	7

Our analysis suggests a direct relationship between total patch dosage and *mean* postmortem fentanyl concentration up to the 100- $\mu\text{g}/\text{h}$ dose, but the very large standard deviations and overlapping ranges effectively nullify the utility of correlating the dose and expected postmortem concentration for any particular death. In other words, one would not be able to reasonably predict the expected postmortem fentanyl concentration based solely on the dose of the patches on the body. Conversely, one would not be able to reasonably extrapolate the dose received solely from the postmortem fentanyl concentration. Importantly, the lack of strict correlation between patch dose and postmortem fentanyl concentration complicates the cause of death determination, but it does not render the medical examiner unable to determine the cause and manner of death. As with the determination of any cause and manner of death, toxicology results are only one datum point among several that are considered. Other factors that may take precedence over a postmortem fentanyl concentration when determining cause of death include scene or circumstantial evidence and other autopsy findings. Our study supports the concept that postmortem fentanyl measurements, especially those in the moderate ranges, should be interpreted with great caution and only in conjunction with other information obtained from the death investigation.

Because of the lipophilicity of fentanyl, we hypothesized that postmortem fentanyl concentrations would be higher in obese individuals due to increased postmortem release of fentanyl from adipose tissue. In order to test this hypothesis, we examined the relationship between body mass index and postmortem fentanyl measurements for a single dosage category of 100 mcg/h. Though the least squares line suggests a possible weak direct relationship between body mass index and fentanyl concentration, the data set is small ($n=15$) and there are other limitations (see below). The plotted data points are widely scattered so no definite correlation was found. Andresen et al. have also examined the relationship between body mass index and postmortem fentanyl measurement, and found no definite correlation (29). Further research to determine whether adipose tissue represents a significant depot for postmortem release of fentanyl is warranted.

Limitations

We were unable to assess the degree of tolerance to opioids of any individual patient. The development of tolerance may partly explain some of the extremely high blood concentrations noted in the population. Relatedly, the specific dose of fentanyl that a patient was prescribed, if any, and was using appropriately was not always known. The effects of dose rate of delivery and chronicity of use, duration of postmortem interval, and site of the blood sample may explain some of the variability of blood concentrations. An opioid naïve person started on the initial fentanyl patch may display significantly different postmortem pharmacokinetics (redistribution) than a long-term fentanyl patch user. Since the patches were not analyzed, a decedent with multiple patches may simply have neglected to remove some or most of them following the intended duration of use. Consequently, someone with three patches may have two that contain variable quantities or no fentanyl and only one that contains the drug. Therefore, the precise dosages at the time of death are not known. The relative contribution of co-intoxicants to causing death cannot be known for certain, although in isolation opioids are the class of medications with the most consequential respiratory and lethal effects.

Conclusion

Based on the variable relationship between dose and blood concentration, the antemortem dose cannot be reliably predicted based on the postmortem concentration. This does not fully impair the ability to determine the cause or manner of death since other factors, such as other autopsy findings and circumstances, are available to support the decision making.

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