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Update: Observations on Fentanyl Designer Drugs

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Abstract

We have previously reported the close association of designer fentanyl drugs with the presence of fentanyl. We continued this study by examining the presence of two other fentanyl structural analogs with fentanyl in urine drug tests. Based on drug testing on 1650 patient samples, we observed 119 positives for fentanyl (7.20% positivity), 23 positives for para-fluorofentanyl and 16 positives for despropionyl-p-fluorofentanyl. Both these analogs had a 100% correlation with fentanyl. In addition, we observed 8 urines positive for both xylazine and fentanyl. We do not know the source of the designer fentanyl analogs, but it appears that testing for fentanyl alone is adequate to detect fentanyl abuse.

Keywords: Fentanyl; Designer drugs; Drug testing; Fentanyl analogs

Background

One of the purposes of illicit designer drugs is to avoid detection by the usual urine drug testing methods. As a consequence, laboratories set up methods to detect these compounds. Analytical methods using LC-MS/MS methods can detect targeted designer drug derivatives of cannabinoids, benzodiazepines, and synthetic opioids such as fentanyl. There has been much interest in fentanyl analogs being present in substance abuse users [1-5]. Because of the specificity termed targeted testing, the laboratory is limited to a short list of designer drugs so it must be selective to detect the most prevalent ones [6]. The state of Massachusetts MADDS program identified two fentanyl analogs prevalent in its substance abuse users: para-fluorofentanyl and despropionyl-p-fluorofentanyl [7]. In addition, the CDC [8], and the State of Michigan [9], observed many overdose deaths associated with the p-fluoro analog. We examined a number of specimens from rehabilitation programs to

determine the association of these two analogs with fentanyl.

Methods

This study was approved by WCG IRB Puyallup, WA. Convenience specimens from rehabilitation facilities were tested using a modification of the method of Krock et al. [10,11]. The standards were obtained from Cerilliant and Cayman Chemical. The Sciex instruments were set at 355.2 m/z for the parent para-fluorofentanyl, and the qualifier ion set at 105.1 m/z and the quantifier at 188.2 m/z. For the despropionyl-p-fluorofentanyl, the instruments were set at 299.4 m/z for the parent despropionyl-p-fluorofentanyl, and the qualifier ion set at 105.2 m/z and the quantifier at 188.4 m/z. The precursor, quantifier, and qualifier ions are listed in Table 1. The data was assembled using previously reported method [12].

Table 1: MRM transitions and cutoffs for fentanyl and its analogs.

	Precursor Ion (m/z)	Quantifier Ion (m/z)	Qualifier Ion (m/z)	Cut-off (ng/mL)
Fentanyl	337.446	188.1	105	1
para-fluorofentanyl	355.2	188.2	105.1	2
Despropionyl-p-fluorofentanyl	299.4	188.4	105.2	2

Results

Based on drug testing on 1650 patient samples, we observed 119 positives for fentanyl (7.20% positivity), 23 positives for para-fluorofentanyl and 16 positives for despropionyl-p-fluorofentanyl, both these analogs had a 100% correlation with fentanyl. In addition, we observed 8 urines positive for both xylazine and fentanyl.

We observed a large difference in the mean fentanyl concentrations between the ones positive for the p-fluoro and those

not positive. Those positive for p-fluoro have much greater fentanyl concentrations 544 ng/mL and about 198 ng/mL for the negative ones. The incidence of designer fentanyl compounds was observed only about 10% of the time.

Table 2 shows the frequency of the designer fentanyls and fentanyl. Both the parent drug and its analog always occurred together. The analogs were always present at lower concentrations. These lower concentrations are consistent with the possibility that these were added separately.

Table 2: Summary data for Fentanyl, para-fluorofentanyl, Despropionyl-p-fluorofentanyl.

Calculated Concentration (ng/mL)			% FluoroAnalog / Fentanyl	
Fentanyl	para-fluorofentanyl	Despropionyl-p-fluorofentanyl	% para-fluorofentanyl / Fentanyl	% Despropionyl-p-fluorofentanyl / Fentanyl
464	32	3	6.87%	0.63%
177	27	6	15.23%	3.46%
112	34	3	30.20%	3.02%
579	12	3	2.05%	0.50%
431	10	2	2.38%	0.53%
354	43	2	12.07%	0.65%
1125	358	21	31.78%	1.86%
193	16	8	8.39%	3.91%
2123	212	46	9.99%	2.16%
1207	25	23	2.04%	1.91%
1097	9	5	0.78%	0.45%
207	12	8	5.92%	4.06%
140	5	3	3.68%	1.85%
652	12	6	1.85%	0.98%
34	3		9.94%	
659	3		0.44%	
140	4		2.62%	
760	2		0.29%	
33	3		8.99%	
73	3		4.01%	
483	4		0.82%	
1672	8		0.46%	
309	2		0.77%	
13	4		31.12%	
567	2		0.35%	
		-		-

Discussion

The observations of the presence of these compounds from sources such as the Massachusetts MADDs program, the CDC Morbidity and Mortality letter, and the Michigan death study would indicate this compound is a major problem [7-9]. These studies would indicate that laboratories should be set up to monitor these designer analogs. The data presented here indicates that the presence of fentanyl itself is a good indicator of illicit drug use.

We do not know the source of these analogs. Because of their low concentrations compared to fentanyl, one possibility is that they are made from poorly sourced fentanyl precursors. A second possibility is that the addition of these compounds enhances the opiate high, although the pharmacogenomics in humans is not well known [13]. The Massachusetts Drug Supply Data Stream (MADDs) report states that the 4 fluorofentanyl has a higher toxicity risk than fentanyl [7]. Because our data is consistent with the p-fluoro analog being added to the fentanyl supply as an additive we favor this explanation.

Acknowledgement

None.

Conflict of Interest

Author declared no conflict of interest.

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