Trakia Journal of Sciences, Vol. 10, Suppl. 2, 311-313, 2012

Available online at:
http://www.uni-sz.bg

ISSN 1313-7050 (print)
ISSN 1313-3551 (online)

A CASE OF COMBINED INTOXICATION WITH FENTANYL AND MIDAZOLAM

D. Nikolov*, Al. Anastasova, St. Hristov, Al. Alexandrov, A. Christov, M. Goshev, I. Brainova, T. Kiryakova

Department of Forensic Medicine and Deontology, Medical University, Sofia, Bulgaria

ABSTRACT

A rare case of combined poisoning of 44-years old woman is presented. The deceased woman washis working as an anesthesiology nurse. According to data of her family, the woman had long time complained of pain in the spine for undisclosed reasons. During the observation at the crime scene at the home of her boyfriend, where she was found dead on the kitchen floor, there were empty ampules of Fentanyl and Midazolam and used syringe and needle found in the garbage bin. During the forensic medical autopsy and forensic toxicological examination of blood, urine and visceral organs an acute poisoning with Fentanyl and Midazolam was proved.

Key words: intoxication, Fentanyl, Midazolam.

INTRODUCTION

Fentanyl is a potent opioid analgesic with synonymous Sentonyl, Fentanil, Fentanylcitrat, Fentanyli citras, Fentanyl citrate, Fentanest, Haldid, Leptanal, Sentonyl, Sublimaze, piperidine derivative with full systematic name (by IUPAC system) N-(1 - (2-phenethyl) 4-piperidinil-N-phenil-propanamide **(Figure 1)**.

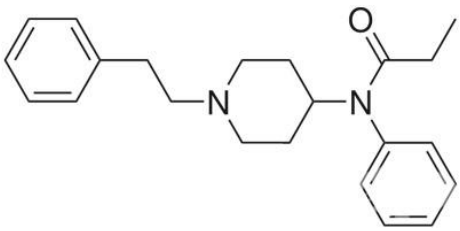

Figure 1. Molecular structure of Fentanyl

Fentanyl is a potent narcotic analgetic affecting predominantly μ-opioid receptors. Besides pain relief, fentanyl causes drowsiness and euphoria, but these effects are less stringent in comparison with heroin and morphine. Like other narcotic derivatives the use of fentanyl may result in respiratory dysfunction to apnea, muscle rigidity affecting and chest muscles, myoclonus, bradycardia, hypotension, nausea, dizziness, vomiting, fatigue, headache, constipation, anemia and peripheral edema. The tolerance and addiction develop quickly after repeated use.Characteristic withdrawal symptoms are sweating, anxiety, diarrhea, bone pain, abdominal cramps and chills of the skin. Serious interactions may occur when combining fentanyl with heroin, cocaine, alcohol and other CNS depressants such as benzodiazepines and midazolam. Overdose leads to respiratory depression and sudden death may occur due to primary cardiac arrest due to severe anaphylactic reaction or laryngospasm.

Lethal dose of fentanyl is in the range 0,0003-0,003 mg%.

Many of the death cases were caused by misuse of pharmaceutica products. Fentanyl is distributed in the form of injection, transdermal patches and buccal tablets. Non-pharmaceutical (crime) fentanyl administration is committed by injection, tablets (designer drugs), transmucosal administration - rubbing inbuccal mucosa, sniffing the powder through

***Correspondence to**: *Dimitar Nikolov, MD, Medical University, Sofia-1431, Bulgaria, Department of Forensic Medicine and Deontology, 1 Georgi Sofiiski blvd. Tel: +35929230764, Fax: +35929230412, E-mail: di.ni.ni@abv.bg*

the nostrils, smoking fentanyl infused with cigarette paper.

Mizazolam is a medicinal product belonging to the group of benzodiazepines, fully systematic name (by the IUPAC system) 8-chloro-6-(2-fluorfentanil)-1-methyl-4 H-imidazo / 1,5-2a / / 1 4 /benzodiazepine **(Figure 2).**

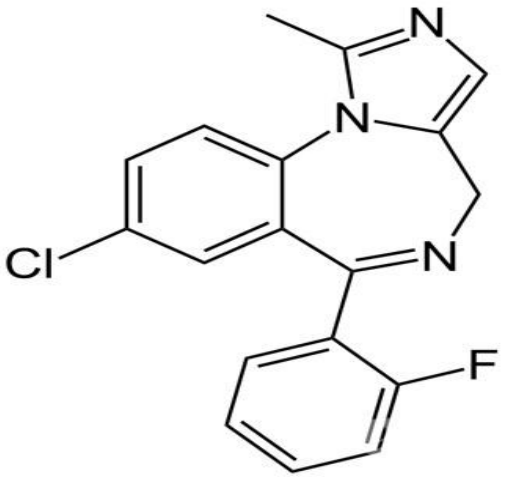

Figure 2. Molecular structure of Midazolam:

Midazolam has anxiolytic, amneztichen, hypot ensive, anticonvulsantand sedative effects. Undesirable drug reactions are allergic reactions, confusion, depression, anxiety, agitation, irritability, aggression, delusions, hallucinations, ataxia, double vision, gastrointestinal complaints, muscle weakness, shortness of breath. Midazolam interacts with barbiturates, antihypertensives, ritonavir, neuroleptics, antidepressants, vasodilators, antispasmodics, opioid analgesics, general anesthetics, rifampicin, alcohol, and potentiate their effects. Toxic dose of midazolam is 0.1 to 0.15 mg%.

MATERIALS AND METHODS

Forensic medical autopsy, toxicological analysis of samples of blood, urine, kidney, liver, stomach and small intestine with their contents.

RESULTS

Toxicological analysis of the samples of blood, urine, kidney, liver, stomach and small intestine with their contents revealed the following – **table 1**.

***Table 1.**: Toxicological analysis of the samples*

Sample	Midazolam	Fentanyl
Blood	0,0600mg%	0,0029mg%
Urine	----------	Insignificant quantities
Kidney	Insignificant quantities	0,0040mg%
Liver	Insignificant quantities	0,0055mg%
Stomach, small intestine and contents	Insignificant quantities	0,0025mg%

Macroscopic autopsy findings revealed morphological signs of rapid onset of death. There were no pathological changes or traumatic injuries that could lead to a fatal outcome. There were injection stitches in thighs and right arm a different timing - new and old.

The established concentrations of fentanyl in the blood and internal organs highly exceed the therapeutic dose of the drug.

CONCLUSION

The autopsy data (morphological findings of sudden death, lungs and cerebral edema, dark liquid blood, intensive livores mortis and injection stitches and the results of toxicological analysis, compared with data from the crime scene give basis to be concluded that in this case the cause of death is acute poisoning with the drug Fentanyl in combination with Midazolam. The result of this drug combination was paralysis of vital brain structures, development of acute respiratory and cardiac dysfunction and sudden death.

Researching the specialized medical and toxicological literature in the Republic of Bulgaria, we havenot found case reports of such acute poisoning with the drug Fentanyl applied in lethal doses. It is a case of poisoning with the drug Fentanyl as a pharmacological

agent used in anesthesiology and reanimation practice.

In the present case is a case of chronic use of opioid analgesic which has about 80 times higher potent than heroin by very narrow margins between tolerance and toxicity. Forensic medical and forensic toxicological stresearches gave grounds for discussion and implementation of appropriate methodologies for toxicological examination and a standard of comparison for poisoning with the drug Fentanyl.

REFERENCES

1. Denton, J.S., Donoghue, E.R., McReynolds, J. and Kalelkar, M. (2008), 'An epidemic of illicit fentanyl deaths in Cook County Illinois: September 2005 through April 2007', *Journal of Forensic Sciences*, Volume 53, Issue 2, pp. 452–454.
2. Henderson, G. (1991), 'Fentanyl-related deaths: demographics, circumstances and toxicology in 112 cases', *Journal of Forensic Sciences*, Volume 36, Issue 2, pp. 422–433.
3. Higashikawa, Y. and Suzuki, S. (2008), 'Studies on 1-(2-phenethyl)-4-(N-propionylanilino)piperidine (fentanyl) and its related compounds. VI. Structure-analgesic activity relationship for fentanyl, methyl-substituted fentanyls and other Analogues', *Forensic Toxicology*, Volume 26, No 1, pp. 1–5.
4. Hull, M.J., Juhascik, M., Mazur, F., Flomenbaum, M.A. and Behonick, G.S. (2007), 'Fatalities associated with fentanyl and co-administered cocaine or opiates', *Journal of Forensic Sciences*, Volume 52, Issue 6, pp. 1383–1388.
5. Jones, T.S., Krzywicki, L., Maginnis, J., et al. (contributors) (2008), 'Nonpharmaceutical fentanyl-related deaths – multiple States, April 2005–March 2007', *Morbidity and Mortality Weekly Report*, Volume 57, No 29, pp. 793–796, Centers for Disease Control and Prevention, USA.
6. Kronstrand, R., Druid H., Holmgren, P. and Rajs, J. (1997), 'A cluster of fentanyl-related deaths among drug addicts in Sweden',*Forensic Science International*, Volume 88, No 3, pp. 185-195.
7. Moffat, A.C., Osselton, M.D. and Widdop, B. (editors) (2004), *Clarke's Analysis of Drugs and Poisons*, 3rd edition, Volume 2, Pharmaceutical Press, London.
8. Sweetman, S.C. (editor) (2007), *Martindale: the complete drug reference*, 35th edition, Pharmaceutical Press, London.
9. United Nations (2006), *Multilingual Dictionary of Narcotic Drugs and Psychotropic Substances under International Control*, United Nations, New York.
10. Woodall, K. L., Martin, T.L. and McLellan, B.A. (2008), 'Oral abuse of fentanyl patches (Duragesic®): seven case reports', *Journal of Forensic Sciences*, Volume 53, No 1, pp. 222–225.
11. The Bulletin of TIAFT, volume 26 number 1 Supp