

Revisit of a Rare Death by Overdosed Midazolam: A Forensic Pathological Perspective

John Z Wang^{1*} and Liming Wang²

¹California State University, Long Beach, USA

²Forensic Science Institute of Dalian, China

*Corresponding author: John Z Wang, California State University, Long Beach, USA, E-mail: zwang2@csulb.edu

Received date: January 25, 2018; Accepted date: February 15, 2018; Published date: February 22, 2018

Copyright: © 2018 Wang JZ, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Midazolam has long been employed for sedation and analgesia purposes in medical surgeries. However, this case re-evaluation reports a rare death case by overdosed midazolam to demonstrate a complex murder plot in Dalian, China. Specifically, this research project analyses and re-evaluates the original investigation report, the original autopsy report and the examiners' findings. Based on the case analysis, the pathological examination indicates that a high concentration of midazolam (9.73 µg/ml) was tested in six needle mark areas (on the left arm and left/right buttock areas). The concentrations were determined and confirmed by LC/MS and GC/MS. This rare case strongly suggests that overdosed midazolam can be intravenously administered as a means of criminal homicide. This case was considered to be the first case reported by the forensic medicine community in China, which might indicate that overdosed midazolam may indicate a new means of killing in years to come. This research project may suggest three practical implications from a forensic pathological perspective. First, this analysis serves as a warning to the medical community that midazolam may have a dangerous side effect, if improperly administered. Second, several reports have indicated that overdosed midazolam can cause deaths. Finally, there has been a real case reported in China where overdosed midazolam was used to kill in a murder case with a concentration of midazolam (9.73 µg/ml) found in muscular areas (the needle marks) by the autopsy findings.

Keywords: Forensic medicine; Autopsy; Cause of death; Manner of death; Murder; Midazolam; LC/MS; GC/MS; Forensic pathology

Introduction

In December of 2009, a young woman was found dead in a hotel room in Dalian, China. The local police department initially could not determine at the beginning the cause of death nor manner of death because there were no physical signs of obvious injuries by blunt or sharp instruments on her body. According to the hotel reservation staff, the room was booked two days earlier by a doctor from Taiwan who left the hotel without checking-out. The investigators immediately turned to the surveillance cameras inside and around the hotel. Although the suspect was soon identified, he managed to flee to Taiwan. As a result, four legal and forensic questions remained challenging to local authorities. First, the medical examiners had to produce sufficient pathological evidence of proof that the suspect committed the murder. Second, the cause of death must be established to prove what led to her death medically. Third, the manner of death must prove to be a homicide, a suicide, or an accidental death due to the existing circumstances. Finally, the corpus delicti of a criminal act, criminal intent, and the relationship between the act and the intent were required for a further legal course. Due to the unique circumstances of the case, the authors decided to revisit this rare case and summarize the unusual medical conditions found during the autopsy process. Hopefully, this case re-evaluation may provide useful information to the fields of forensic pathology, forensic toxicology as well as forensic medicine.

Methodology

There has been a lack of literature on midazolam in criminal cases [1]. To revisit the unique case, this case re-evaluation follows three steps: 1) Reviewing the criminal investigation report, 2) Reviewing the autopsy report during the medical examination process, and 3) Conducting a case re-evaluation of the autopsy report.

Reviewing the criminal investigation report

The victim was a Chinese female, 23 years old, born in November of 1986. She worked as a fashion sales-woman and later as a hotel worker in Dalian, China. The criminal investigation discovered that the suspect and the victim had been in a mistress relationship for two years although the suspect was married in Taiwan. The suspect was a doctor and born in March of 1970. On the day of the incident, from the surveillance cameras footage the suspect went to a nearby grocery store cross the street between 2 P.M. and 2:40 P.M. and purchased three different types of liquors. The young woman remained in the hotel room and did not go out. From the surveillance cameras inside the hotel, the suspect went down from the 14th floor and went through the fire corridor around 7:39 P.M. He had dinner downstairs and returned to his room around 8:31 P.M. The suspect was then seen walking out of the room with his red carry-on luggage, a black suitcase, and a white bag and left the hotel without checking out. The suspect was seen getting into a taxi. Around 10:39 P.M. the suspect took another taxi from another location of the city and eventually arrived in the airport, however, the white bag was missing. Around 12:55 A.M., the next day the suspect flew from Dalian to Hong Kong. At 9:00 A.M. next morning, the hotel reported the death of the female victim. From the surveillance camera system, the evidential fact that the doctor was with

the victim at the time of the incident was established and he became the primary suspect in the case. However, more evidence is needed from an autopsy for the cause of death and the manner of death.

Reviewing the autopsy report

The medical examiners must determine the cause of death from an autopsy and the manner of death, if possible. An autopsy report is a post-mortem evaluation of a person's body to examine physical markings, internal fluids, and organs to determine the cause of death. In this particular case, three medical examiners and two toxicologists performed the autopsy to limit the possibilities of errors. The following steps and related analyses were performed in January 2010 in Dalian, China.

External exam: The deceased was 166 cm in height with a normal nutrition condition. The rigor mortis on the back and both sides of the body appeared to be purple. There were pressure changes on the body's left side, suggesting to the medical examiners that the body was originally resting on the left side. However, the rigor mortis began to be softened since light red spots could be observed in both eyeballs. The opacity of the cornea existed already. The sagittal diameter of both pupils was measured at 5 mm. The mouth and ear cavities, and the teeth and gum seemed to be normal. The neck and the chest were symmetrical with the windpipe in the middle. There were red artificial red nails on her ten fingers. Her abdomen was flat, and her vaginal and anal areas appeared to be without any injuries.

The woman's hair was medium length and varied from shades of light black to dark black. The victim's eyes were black and slightly dilated. However, there was a red bruised red spot (5 mm × 5 mm) on the top of her right eye. Another two bruised areas (10 mm × 5 mm and 3 mm × 5 mm) were also noticed below her left lower lip. On her right back, there were several long but shadow cuts. Most importantly, there was a small needle mark with a purple colour edge on her left upper arm. On her left lower inner arm, several purple bruises with an oval shape could be observed. On her left hand and wrist areas, more bruises (around 3 mm × 3 mm and 5 mm × 5 mm) were also noticed. On her right outer side arm, one could see an obvious long bruised area (10 mm × 5 mm). There was a clear bite mark in a crescent shape located on the root of her right outer thumb. There were several needle marks on her arm and buttock areas that punctured through subcutaneous tissues and skin surfaces. In particular, six needle marks were located on her body: one on the left upper arm (2 mm × 2 mm) (Figure 1), one on the right upper buttock area (8 mm × 2 mm), three needle marks on the left lower buttock area (3 mm × 2 mm each) (Figure 2), and one on her right upper buttock area. Finally, there were several bruised areas visible on both of her legs. The next part of the process was the internal examination in which the medical examiners cut into the body and analyse the body fluids.



Figure 1: One needle mark was found on the left upper arm (2 mm × 2 mm).

Internal examination: The pathologists began with a Y-shaped incision. There were two accumulations of blood underneath the left forehead area (20 mm × 10 mm and 20 mm × 5 mm). No other internal haemorrhages were visible inside the skull cavity. No fluid was seen in the abdominal or thoracic spaces. All organs appeared normal. Next, the medical examiners looked at the respiratory system. There was slight congestion of mucosa and accumulation of blood in the victim's larynx, trachea, and bronchi. Some foamy material was found in the upper portion of the trachea, which was observed to continue down toward the lower portion of the trachea. The neck bone was intact. The medical examiners found some partially digested food particles and some fluids in the stomach. Some haemorrhage was found in both lungs. The lacerated surfaces showed congestion and edema without visible haemorrhage or consolidation. All pulmonary vessels were normal. There were no distinguishable abnormalities noted in the uterine, tubes, or ovary systems.



Figure 2: Three needle marks were found on the left lower buttock area.

Pathological examination: There was haemorrhage spots in the blood capillary system and the nerve cells in the brain stem appeared to be swollen, both of which were indicative of a lack of oxygen and blood circulation at the time of death.

The analysis of the cardiovascular system and the coronary arteries showed that the aorta and aortic branches appeared to be swollen. The veins inside the lung were also swollen with haemorrhage. The blood capillary systems in the heart, liver and kidneys were either seen to have been swollen or with blood spots. However, the hemic, the lymphatic, the urogenital (tubes or ovaries), the pancreas and the endocrine systems appeared to be normal.

Toxicological examination: The final portion of the autopsy is a toxicology report, in which specimens of the heart, stomach contents, liver, and muscular areas (needle marks) were submitted for studies. The only substances found in the victim's toxicology report were 0.22 µg/ml of midazolam in the cardiovascular system, 0.41 µg/g in the stomach system, 0.06 µg/ml in the liver system and 9.73 µg/ml in the six needle mark areas. No alcohol was found in the cardiovascular system, but in the stomach content, a concentration of 30.56 µg/g of alcohol was tested. Obviously, the concentration of overdosed midazolam (9.73 µg/ml) in muscular areas (the needle marks) was much higher than those of other systems in the body (Figure 3). All the tests on the concentrations were performed and confirmed by LC/MS and GC/MS.



Figure 3: Sample of the prescription drug of Midazolam.

After performing the autopsy, the medical examiners were able to produce a summary of the autopsy results by focusing on the six needle marks on the arm and the buttock areas. Therefore, based on the toxicological findings from the autopsy, the victim's cause of death was determined to be injections of overdosed midazolam. Further, the toxicological examination concludes that there were varying degrees of midazolam concentrations of 0.22 µg/ml in the cardiovascular system, 0.41 µg/g in the stomach system and 0.06 µg/ml in the liver system. The existence of 0.41 µg/g of midazolam in the stomach system indicates that she had some drinks mixed with midazolam, which in turn results in the existence of midazolam in cardiovascular system and in the liver system by the digestion process. Next, the six needle marks suggest that the injections or administrations of midazolam

were conducted multiple times, meaning that the criminal acts (injections) could last over a couple of hours. Finally, various bruised areas on her body may prove to be some rough sexual acts or the subduing acts between the two. All the symptoms and findings from the autopsy report strongly indicate the suspect's deliberation and premeditation of murdering the female victim or his mistress.

Conducting a case re-evaluation of the autopsy report

Midazolam has long been employed for sedation and analgesia purposes in medical surgeries. It is reported that people died after being injected with wrong doses of the sedation and another 48 people were harmed after receiving an overdose of the drug used to sedate patients during procedures [2,3].

From a pharmacological point of view, midazolam slows down both the heart and lung rate and is thus used for conscious sedation. It is often given to people who need tubes insertion during endoscopies or for minor surgery. However, the drug can induce amnesia and cause a heart attack or decreased lung function when given in very high doses. As a result, the National Patient Safety Agency (NPSA) warned of its potential risks for three situations [4]. First, the presentation of high-strength midazolam as 5 mg/ml (2 ml and 10 ml ampoules) or 2 mg/ml (5 ml ampoule) may exceed the dose required for most patients. Second, there is a risk that the entire contents of high-strength ampoules are administered to the patient when only a fraction of this dose is required. Finally, if the doses exceed those required, not titrated to the patient's individual needs, the situation may also fail to take into account any concurrent medication and may affect high-risk groups, for example, the frail or the elderly [5,6].

Midazolam may be the ideal drug for use in many interventional procedures because it has a rapid onset of action (usually less than 3 min) and a short duration of effect (usually less than 60 min) [7]. Unfortunately, a rare case by overdosed midazolam was reported here to demonstrate a complex murder plot in Dalian, China. A high concentration of midazolam (9.73 µg/ml) was tested in the six needle mark areas (on the left arm and buttock areas, and the right buttock area). The concentrations were determined and confirmed by LC/MS and GC/MS. This case analysis strongly suggests that overdosed midazolam can be intravenously administered as a means of criminal homicide.

Midazolam is a short-acting BZD, whereas the onset of its effect is within 2 min and it lasts between 45 and 60 min [7]. The short-acting sedative effect with rapid recovery, the low risk of respiratory depression, and the ante-grade amnesic effects associated with midazolam make it the favoured sedative agent used by non-anaesthesiologists to achieve moderate sedation during radiology procedures [6]. Although this agent is relatively safe, more than 80 deaths have been reported after midazolam use for patients undergoing a variety of medical and surgical procedures [8]. Due to the excellent work of forensic medical examiners in the case, the suspect was convicted of the murder for 11 years in prison in Taiwan.

The overall criminal investigation supported the cause of death and the manner of death from the autopsy, pathology and toxicology reports in five aspects. First, the surveillance camera systems proved that the suspect did not have an alibi because he was with the victim during the whole incident (no third person). Second, the fingerprints developed from the hotel room indicated that he was present at the crime scene. Third, from the police interviews, the grocery owner was able to identify the suspect to be the person who had purchased three

different types of liquors for drugging her. Next, the police in Taiwan was able to restore the deleted images from his video camera with which he used during the incident. The deleted image showed his drugging, sexual and violent acts on the victim. Finally, due to all the evidence presented at trial, the suspect partially confessed his acts. There was one disagreement: the criminal investigation suggested that those bruised areas around her mouth and on other areas of the body could be a result of suffocation by some soft fiber substance, which could be some supplementary acts to the overdosed midazolam. However, there were no fibre residues that were detected in her mouth, nose and inside her larynx, trachea and bronchi.

Conclusion

This rare murder case by the favoured sedative agent midazolam has been reported with detailed information on its autopsy process and the medical examiners' findings. This case analysis may suggest three practical implications from a pathological perspective. First, this analysis serves as a warning to the medical community that midazolam may have a dangerous side effect, if improperly administered. Second, several reports have indicated that overdosed midazolam can cause deaths. Finally, there has been a real case reported in China where midazolam was used to kill in a murder case with a concentration of midazolam (9.73 µg/ml) found in muscular areas (the six needle marks) by autopsy findings.

Acknowledgement

The authors would like to express our sincere appreciations to the Forensic Science Institute of Dalian, China for the support to this research project.

References

1. Michalodimitrakis M, Christodoulou P, Tsatsakis A, Askoxilakis I, Stiakakis I, et al. (1999) Death related to midazolam overdose during endoscopic retrograde cholangiopancreatography. *Am J Forensic Med Pathol* 20: 93-97.
2. Yaster M, Nichols DG, Deshpande JK, Wetzel C (1990) Midazolam-fentanyl intravenous sedation in children: Case report of respiratory arrest. *Pediatr* 86: 463-467.
3. Bailey PL, Pace NL, Ashburn MA, Moll JW, East KA, et al. (1990) Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. *Anesthesiology* 73: 826-830.
4. Kim T (2006) Safety and effectiveness of moderate sedation for radiologic non-vascular intervention. *Korean J Radiol* 7: 125-130.
5. Ben-Shlomo I, Abd-el-Khalim H, Ezry J, Zohar S, Tverskoy M (1990) Midazolam acts synergistically with fentanyl for induction of anesthesia. *Br J Anaesth* 64: 45-47.
6. Cragg AH, Smith TP, Berbaum KS, Nakagawa N (1990) Radomized double-blind trial of midazolam/placebo and midazolam/fentanyl for sedation and analgesia in lower-extremity angiography. *AJR Am J Roentgenol* 157: 173-176.
7. Ayre-Smith G (1987) Fentanyl and midazolam: An alternative to diazepam. *Radiol* 164: 285.
8. Martin ML, Lennox PH (2003) Sedation and analgesia in the interventional radiology department. *J Vasc Interv Radiol* 14: 1119.