

CASE REPORT

Legal issues in patient management of intoxicated patients: a case of auto-intoxication by intravenous pentobarbital injection

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Abstract

We present a case report of a 79-year-old woman who injected herself with pentobarbital. After admission to hospital, laboratory examination revealed a lethal serum concentration of pentobarbital (33 mg/L; toxic serum level > 10mg/L) in the patient. This case of a pentobarbital overdose illustrates that legal issues, such as the authenticity of a written patient statement, have to be considered in decisions on the continuation or discontinuation of curative care.

Introduction

Barbiturates are drugs with sedative and anti-convulsive properties. Barbiturates can be classified into three groups: a) ultra-short-acting (for example thiopental), b) short-acting (for example pentobarbital) and long-acting barbiturates (for example phenobarbital).¹ In Western countries, barbiturates are considered obsolete agents for medical treatment. However, phenobarbital is still prescribed as an anti-epileptic drug. Thiopental and pentobarbital are clinically applied for the induction of narcosis and for lowering the intracranial pressure. In addition, barbiturates are used in various veterinary settings.¹ Barbiturates act by suppressing the central nervous system, resulting in severe sedation or coma in cases of overdose. In cases of intoxications, suppression of the central nervous system, hypotension, hypothermia, coordination disorders, respiratory failure and coma are the major clinical symptoms. Both miosis and mydriasis are observed in patients who have been poisoned with barbiturates.^{2,3,4}

We present an interesting pentobarbital overdose case of a woman admitted to our hospital. In this case we had to deal with legal questions before discontinuation of curative care was permitted and a procedure of a non-natural death was started. The questions included doubt on the authenticity of a suicidal note and, how this woman had access to a pentobarbital solution and, consequently, if she had indeed injected herself.

Case history

A 79-year-old woman was found by her general practitioner at home in a coma. A 100 mL brown bottle without label, containing about 2-3 mL of an unknown viscous liquid and crystals were found near the patient, together with a syringe (*figure 1*). A small injection mark and purple spot were observed on her left elbow.

On admission to the hospital emergency department, she had no heart action. The patient was resuscitated. After return of spontaneous circulation, the patient was admitted to the ICU. Her Glasgow coma score was E1-M1-V1. She was in cardiogenic shock with a sinus bradycardia. Both pupils were slightly dilated. Blood and urine samples were collected for toxicology screening. In these samples, the presence of barbiturates was demonstrated as described below.

The initial therapy in the ICU was mechanical ventilation, therapeutically induced hypothermia (32-34°C), and administration of dopamine and norepinephrine. Several hours

Figure 1. Bottle, containing an unknown mixture with precipitated crystals.



after the initiation of this therapy the patient's family arrived. The family produced a statement that included a prohibition to treat her in times of coma. At that time it was not immediately clear whether, on legal grounds, the treatment should be continued or discontinued. Treatment was continued overnight so that the legal consequences of treatment discontinuation could be further explored. The next morning the patient showed characteristics of clinical brain death. Typical brain death characteristics in this patient were the absence of stem reflexes and apnoea. Also an iso-electric EEG was observed. After approval by the public prosecutor, mechanical ventilation was stopped according to the wish of the patient. The patient died because of apnoea within a few minutes. Thereafter, the routine procedure for non-natural death was followed.

Toxicology investigations

After admission to hospital, blood and urine samples were collected for toxicology screening. Toxicology investigations were performed on blood and urine samples and on a bottle found at her house.

Bottle

The bottle contained 2-3 mL of a viscous alkaline liquid mixture with precipitated crystals. Liquid and crystals were investigated by Fourier Transform Infrared Spectroscopy using a Nicolet Avatar 370 DTGS apparatus (Thermo Fischer Scientific, Madison, USA), equipped with a toxicology library and by a HPLC-diode array detection with library (Systematic Toxicological Identification Procedure, STIP,^{5,6,7}) as described below.

Toxicology screening of the liquid and crystals in the bottle indicated the presence of ethanol, propylene glycol and a barbiturate-like compound. The STIP analysis revealed the presence of pentobarbital in the bottle. The pH of the mixture in the bottle was 11. This can be attributed to the presence of the pentobarbital in the form of the sodium salt. The pentobarbital concentration of the liquid in the bottle was 16g/100 mL. This corresponds with a concentration of pentobarbital in the form of the sodium salt of 17% (g/v).

Patient

A comprehensive screening was performed on urine- and serum samples. Considering the clinical state of the patient, the serum was screened for the presence of ethanol, paracetamol, salicylates and metoprolol. The urinary toxicology screen was done by immunochemistry (Emit[®] 2000, Siemens Healthcare Diagnostics Inc., Newark, DE 19714, USA). STIP was performed allowing identification and quantification of toxic compounds.^{5,6,7} A Shimadzu CLASS-VP V 6.12 SP4 HPLC system was used equipped with a Microsphere C18 column (30 cm x 4.6 mm). The mobile phase was a mixture (1000 mL) of acetonitril (Lichrosolv[®]) (470 mL) and water (530

mL), containing phosphoric acid 85% (approximately 400 µL), triethylamine 146 µL, adjusted to pH 3.30 with a 10% (g/v) potassium hydroxide solution. The column temperature was 55°C, the flow rate was 0.6 mL/min and the detection took place at 205 nm. The retention times in minutes were: phenobarbital 3.8; butobarbital 4.4; secobarbital 7.4; pentobarbital 5.9 and thiopental 11.5. Calibration curves were constructed by adding known amounts of pentobarbital and MMPH (5-(p-methylphenyl)-5-phenylhydantoin) as internal standard to methanol or serum.

The toxicology screen did not reveal traces of cocaine, heroin, methadone, amphetamines, cannabis, benzodiazepines, paracetamol, salicylates and metoprolol. The urinary toxicology screen clearly indicated the presence of barbiturates, corresponding with the findings in the bottle found at the patient's house. Only a low level of ethanol was found in her blood (0.14 g/L). STIP analysis confirmed the presence of pentobarbital in the woman's blood and revealed that the serum pentobarbital level was 33 mg/L. Therapeutic ranges of pentobarbital in serum are between 1-10 mg/L. Serum levels above 10 mg/L can cause coma and levels above 30 mg/L as observed in the present case are usually lethal.^{1,2,3}

Discussion

This case demonstrates that legal issues have to be carefully considered in cases of drug overdoses. Legal issues may influence patient management as illustrated in our ICU patient who had injected herself with a lethal amount of pentobarbital. In this case, it was possible to estimate the amount of pentobarbital present in the body and the minimal volume of the pentobarbital mixture that the patient had injected into herself. The volume of distribution (Vd) of pentobarbital is 1 L/kg.⁸ The woman's weight was approximately 70 kg, resulting in a Vd of pentobarbital of approximately 70 L. The estimated amount of pentobarbital in the body at the time of sampling was approximately 2.1 grams. In the present case of a presumed auto-injection with a concentrated pentobarbital solution of 16 g/100 mL, it is possible to calculate that at least 13 mL of a possibly veterinary pentobarbital solution has been injected. Interestingly, other cases have shown the death of individuals after auto-injection with similar doses of pentobarbital.^{3,9} For instance, Romain et al. describe a 51-year old man who was found dead who also had a purple spot at the site of injection. The concentration of the injected pentobarbital mixture was 21.7 mg/L and the estimated amount of injected pentobarbital was approximately 1.6 g.⁹ In our case, after admission to hospital, the physicians were informed about a written statement that included the patient's refusal to be treated in a case of coma. At that point it was not clear whether discontinuation of treatment would be legally allowed. Until it was clear whether curative or palliative care should be provided by the ICU, the treatment was continued

overnight. The next day, the patient showed the critical condition of brain death, including an iso-electric EEG, which may have been induced by the pentobarbital.

An important legal issue of the present case is the authenticity of the patient's written statement including her refusal to be treated for a coma. A written statement of refusal orders a physician to respect the wish of the patient by abstaining or omitting medical treatment. In the specific case of a patient attempting suicide and with a written statement for abstaining treatment, refusal of treatment has to be respected.

In the Netherlands, several laws regulate patient rights. According to article 7:450 paragraph 3 of The Dutch Medical Treatment Contract Act (WGBO), a written statement of refusing treatment made by a patient of 16 years or older, has to be respected and is legally enforceable.¹⁰ This is in agreement with the general rule in article 7:450 paragraph 1 (WGBO) which implies that treatment without permission cannot take place. However, there are some exceptions to this general rule. If there are so called 'serious grounds', a physician is not required to obey the written declaration of the patient (article 7:450 paragraph 3 (WGBO)).¹⁰ Such serious grounds may include uncertainty of the authenticity of the statement itself, doubts about the authenticity of the signature and doubts about the interpretation of the statement.

Only in cases where there are serious grounds, a physician is not required to obey the patient's written declaration of abstaining treatment. The physician should confirm that a declaration of refusal has been written. Given the profound effects, it is desirable that any written statement is genuine, has a signature, is dated and is unambiguous. It should be noted that all of these requirements are not obliged by law or regulations *per se*.¹²

In the present case, the written statement of refusal came to light a few hours after the patient was hospitalized. In such cases it is very hard and often unclear what the physician should do. According to the WGBO, a physician is required in case of an emergency to act and treat the patient as stated in article 466 paragraph 2 (WGBO).¹⁰ The general practitioner of this patient indeed confirmed that the patient had signed a legal statement. Furthermore, the public prosecutor also stated that discontinuation of the treatment was legal. The procedure for a non-natural death was started and since it was concluded that she injected herself no further legal investigations were initiated.

Conclusions

This case of a pentobarbital overdose clearly demonstrates that legal issues have to be taken into account in patient management, especially when decisions on continuation or discontinuation of curative care for intoxicated patients are being made.

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