

A Fatal Case of Acute Butane-Propane Poisoning in a Prisoner Under Psychiatric Treatment

Do These 2 Factors Have an Arrhythmogenic Interaction, Thus Increasing the Cardiovascular Risk Profile?

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Abstract: Sudden death due to inhalation of aliphatic hydrocarbons such as butane and propane is well described in the literature. The main mechanism involved is the induction of a fatal cardiac arrhythmia. This phenomenon is frequently associated with prisoners who accidentally die while sniffing these volatile substances with an abuse purpose. Furthermore, such prisoners are often under psychiatric treatment; specific drugs belonging to this pharmacological class lead to a drug-related QT interval prolongation, setting the stage for torsade de pointes. In this article, we present the case of a prisoner died after sniffing a butane-propane gas mixture from a prefilled camping stove gas canister. The man was under psychiatric drugs due to mental disorders. He was constantly subjected to electrocardiogram to monitor the QTc (corrected QT interval), which was 460 milliseconds long. Toxicological analysis on cadaveric samples was performed by means of gas chromatography (head space) and revealed the presence of butane and propane at low levels. The aim of this article was to discuss a possible arrhythmogenic interaction of QT interval prolongation induced by psychiatric drugs and butane-propane inhalations, increasing the cardiovascular risk profile. In other words, evidence may suggest that prisoners, under these circumstances, are more likely to experience cardiovascular adverse effects. We believe that this study underlines the need to take this hypothesis into account to reduce death risk in prison and any medical-related responsibilities. Further studies are needed to validate the hypothesis.

Key Words: butane-propane poisoning, psychiatric treatment, QTc interval prolongation, sudden sniffing death syndrome, cardiac arrhythmia

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The *N*-butane, a low-molecular-weight aliphatic hydrocarbon, is a colorless and flammable gas used commercially as a fuel source and/or propellant. It is usually mixed with propane to produce fuel. Because *N*-butane is the main component of commercial gas preparations, and being more toxic than propane, its concentration in biological fluids and tissues can be used as a good indicator of an intoxication state. In countries where prison cells are equipped with combustible gas cylinders¹ (eg, Italy and other European countries, Australia, and New Zealand), these gas mixtures are often sniffed by prisoners with an abuse purpose, due to their psychotropic effects. The main cause of death, after inhalation of butane-propane mixtures, is a cardiac substance-induced arrhythmia, though asphyxia, vagal inhibition, and respiratory depression may also be involved.² A factor to be reckoned

with is that prisoners often take lot of psychiatric drugs. As a matter of fact, psychiatric drugs, especially antipsychotics, can determine a QTc interval prolongation, setting the stage for the torsade de pointes (TdP), a polymorphic ventricular arrhythmia that can progress to ventricular fibrillation and sudden death. This kind of arrhythmia is more likely to occur if drug-induced QT prolongation coexists with other risk factors. With regard to that, we present the case of a prisoner, under psychiatric treatment, deceased while sniffing a butane-propane gas mixture contained in the gas cylinder of a camping stove.

CASE REPORT

A 40-year-old prisoner was under psychiatric treatment with chlorpromazine and citalopram due to mental disorders. He was constantly subjected to electrocardiogram to monitor his QTc (corrected QT interval), which was 460 milliseconds long.

On April 15, 2013, the prisoner was found, by his cellmate, lying unconscious on the floor of the cell toilet. He was immediately helped, but he was already dead. During cardiopulmonary resuscitation, a gas odor came from the patient's mouth. An on-the-spot investigation revealed a small camping stove with a gas cylinder containing a butane-propane mixture in the toilet, often used by prisoners to cook in their cells. The prosecutor, after an extensive inquiry and interrogation, excluded any possibility of a violent confrontation around the time of the accident. Forensic autopsy was performed 24 hours later. External examination of the body showed no injuries, and the autopsy revealed just pulmonary edema, without disclosing any preexisting pathological substrate as a possible cause of death.

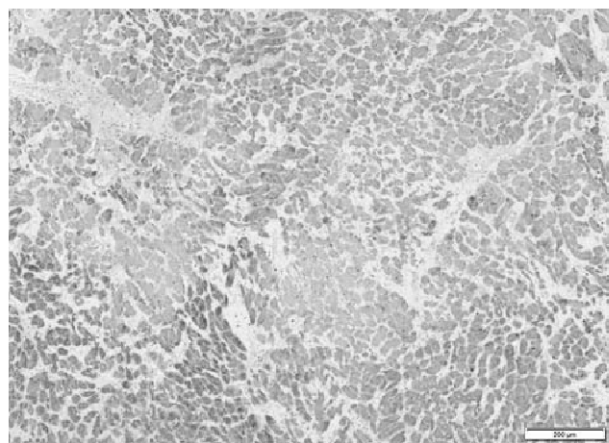


FIGURE 1. Ischemically damaged cardiomyocytes—immunohistochemically detectable loss of myoglobin (internal standard).

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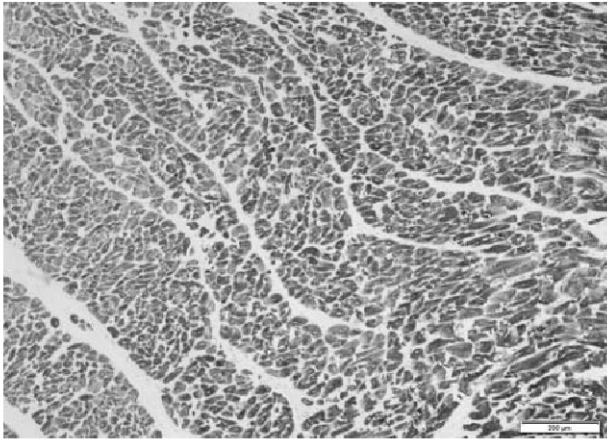


FIGURE 2. Heart sample stained with immunohistochemical agent (myoglobin): cardiomyocytes showing no loss of myoglobin.

Organ and body fluid samples were taken for further analysis. The investigations were completed with a histologic examination of the organs. Specimens were enclosed in paraffin, and 4- μ m-thick sections were cut and stained with hematoxylin-eosin. Preparation of samples from the organs only revealed intra-alveolar edema.

Heart samples were stained by a panel of immunohistochemical agents, myoglobin and desmin (2 main negative markers), and were compared with an internal standard of myocardium showing depletion (Figs. 1-4).

Generally depletion of myoglobin and desmin in myocardial fibers begins within few minutes after the onset of the period hypoxia; in our case, there was no depletion of the 2 immunohistochemical markers, demonstrating so a fast onset of death.

To carry out qualitative and quantitative research on propane, butane, and other toxic gasses, a 1-mL sample of each biological fluid (blood, bile, urine) and 1 g of each organ and tissue (brain, heart, lung, kidneys, spleen, and liver) were taken. These samples were placed separately in hermetically sealed vials with a Teflon lid and metal ring and were incubated in a water bath at 85°C for 15 minutes.

A milliliter of a butane-propane mixture stored in the gas canister found in the cell toilet was simultaneously removed by a

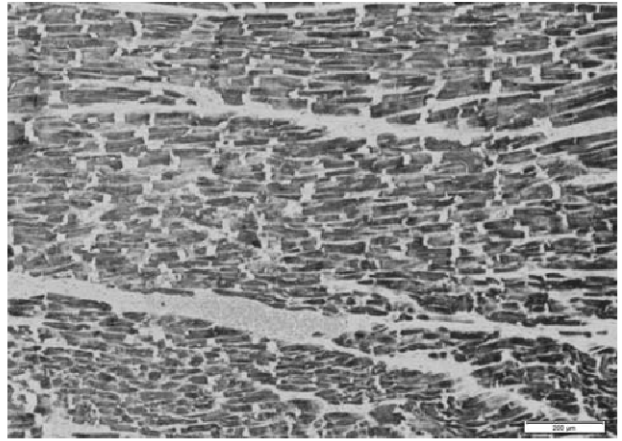


FIGURE 4. Heart sample stained with immunohistochemical agent (desmin): cardiomyocytes showing no loss of desmin.

syringe by inserting the needle thereof in a protection valve and obtaining a standard solution of butane-propane.

Finally, a gas chromatographic technique (head space) analysis was carried out in the following operating conditions: column temperature, 40°C isotherm; injector temperature, 200°C; detector temperature, 250°C; and carrier gas, 12.0 mL/min nitrogen.

The analysis carried out on the samples showed the following concentrations: butane (blood, 0.090 μ L/mL; bile, 0.006 μ L/mL; urine, 0.001 μ L/mL; brain, 0.051 μ L/mg; heart, 0.004 μ L/mg; lung, 0.003 μ L/mg; kidney, 0.004 μ L/mg; spleen, 0.007 μ L/mg; liver, 0.030 μ L/mg) and propane (blood, 0.010 μ L/mL; bile, undetectable μ L/mL; urine, undetectable; brain, 0.026 μ L/mg; heart, 0.002 μ L/mg; lung, 0.001 μ L/mg; kidney, 0.003 μ L/mg; spleen, 0.002 μ L/mg; liver, 0.002 μ L/mg).

Toxicological examinations carried out on central and peripheral blood, tested negative for alcohol, and tested positive for the presence of the antipsychotic drugs usually taken by the prisoner, in therapeutic concentrations (chlorpromazine, 0.27 μ g/mL; citalopram, 0.86 μ g/mL).

In conclusion, the cause of death was referred to a cardiac arrhythmia.

DISCUSSION

Approximately 50% of inhalant-related deaths are due to “sudden sniffing death syndrome,” followed by cardiac arrhythmia.³

The butane-propane inhalation, according to some authors, causes a burst of catecholamines that can trigger ventricular fibrillation.² Furthermore, some authors^{4,5} suppose that butane may sensitize the myocardium to adrenaline, resulting in a fatal arrhythmia.

In our case, toxicological analysis on cadaveric samples, performed by means of gas chromatography (head space), revealed butane-propane mixture in almost all specimens but in low concentration. Our concentrations, lower than those generally described in literature,⁶⁻¹⁰ may be considered sublethal. It is therefore plausible to suppose that some other factor intervened in the determinism of death.

Our toxicological examinations tested positive for the presence of the antipsychotic drugs usually taken by the prisoner in therapeutic concentrations (chlorpromazine, 0.27 μ g/mL; citalopram, 0.86 μ g/mL).

Psychotropic drugs can induce a long QT syndrome, a cardiac conduction disorder characterized by prolongation, and increased dispersion of ventricular repolarization, manifested by lengthening of the QTc interval on the electrocardiogram.¹¹

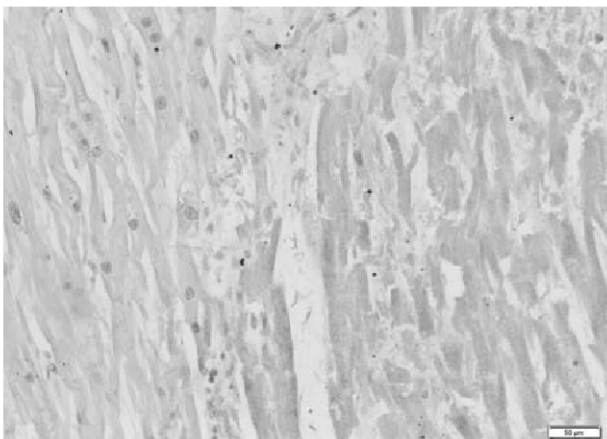


FIGURE 3. Ischemically damaged cardiomyocytes—immunohistochemically detectable loss of desmin (internal standard).

The QTc interval is a heart rate corrected value that represents the time between the onset of ventricles' electrical depolarization and the end of repolarization.

Drug-induced prolongation of the QTc interval usually results from concentration-dependent blocking of the rapid component of the delayed rectifier K⁺ current, which physiologically allows the rapid potassium outflow^{12,13} and the repolarization of cardiomyocytes.

The degree of QTc prolongation varies between psychiatric drugs, reflecting their different capacity to block the delayed rectifier K⁺ current.

A QTc interval prolongation sets the stage for the TdP, a polymorphic ventricular arrhythmia that can progress to ventricular fibrillation and sudden death; an absolute QTc interval of more than 500 milliseconds or an increase of 60 milliseconds from baseline is regarded as indicating an increased risk of TdP.¹⁴

However, TdP can occur with lower QTc values if drug-induced QTc prolongation coexists with other risk factors, such as presence of congenital long QT syndromes, heart failure, bradycardia, old age, hepatic or renal impairment, slow metabolizer status,¹⁴ hypokalemia, abnormal T wave morphology, hepatitis C virus infection, and human immunodeficiency virus infection.¹⁵

We reported a QTc interval of 460 milliseconds, resulted as slightly lower than the high-risk threshold value sets for TdP (500 milliseconds).

Therefore, based on these findings, given the sublethal concentration of butane-propane mixture and the subthreshold value of QTc, it is reasonable to suppose that both synergized and so increasing the arrhythmogenic effect with deadly consequences.

As a matter of fact, TdP is more likely to occur for shorter QTc, if the drug-induced prolongation coexists with other risk factors.

In light of what we have shown up to this point, we supposed that inhalation of butane-propane mixture can be pointed as a risk factor with additive effect, which contributes to TdP occurrence for subthreshold QTc given values.

Even if further studies are needed to evaluate our hypothesis, we believe that this possibility should not be underestimated and therefore combustible gas cylinders should be removed from prison cells to reduce the risk of accidental deaths inside prisons, where inmates are often under psychiatric treatment.

CONCLUSIONS

Acquired long QT syndrome is an iatrogenic disorder, usually induced by psychiatric drugs, which can cause life-threatening arrhythmias. Therefore, drug-induced effects on the QT interval have become a main issue for the practitioner and the regulatory agencies.

The problems related to prolonged QT interval should also be considered among the prisoners, a population showing risk factors (such as human immunodeficiency virus and hepatitis C virus infections) that have been associated with an increased risk of TdP.

With regard to that, we bring to attention the possibility of an arrhythmogenic interaction between psychiatric drugs and the sniffing of butane-propane mixtures, contained in the gas cylinders of the camping stove, often present in the prison cells.

If the postulated mechanism is confirmed, some precautions (such the removing of camping stoves in cells) should be taken to reduce accidental deaths inside prisons.

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