An Unusual Trichloroethanol Fatality Attributed to Sniffing Trichloroethylene

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Abstract

We report the death of a 28-year-old man due to sniffing a contact cement containing trichloroethylene. Initial testing revealed the presence of 80 mg/L trichloroethanol in cardiac blood, and the death was ruled as being due to trichloroethanol toxicity resulting from chloral hydrate ingestion. However, further investigation of the case revealed that the trichloroethanol resulted from trichloroethylene abuse. Subsequent targeted analysis for trichloroethylene, four months after the death, confirmed its presence in cardiac blood (1.1 mg/L), bile (4.5 mg/L), and liver (2.5 mg/kg). Trichloroethanol was initially detected during routine drug screening that employed gas chromatography (GC) using an HP-5 column with electron capture detection and subsequently quantitated by GC using the same column as for the initial screen, but with flame-ionization detection (FID); ethchlorvynol was the internal standard. Trichloroethylene was quantitated by headspace GC with a Restek Rtx-BAC1 column and FID; 1,1,1-trichloroethane was the internal standard.

Case History

A 28-year-old male was found dead on a mattress on the floor of his home, the morning after he was reported to have consumed a large amount of liquor, as well as “sniffing glue”. Later, a nearly empty can of commercial contact cement was located in a garbage can in the house. An autopsy was ordered, and the findings were unremarkable. Cardiac blood and other specimens were collected for toxicology testing.

Toxicology testing initially indicated only the presence of the trichloroethanol; ethanol and other drugs were not detected. Based on the history, a routine screen for “solvents” was performed, but none were initially detected. Given that a sufficiently high concentration of trichloroethanol was detected to account for death, the issue of solvent abuse was not pursued further on the basis that it was unlikely to relate to the immediate medical cause of death.

Four months later, the laboratory received a call from police investigators stating that the decedent’s family was upset that toxicology results implied that the man had overdosed on chloral hydrate. The family stated unabashedly that he had been abusing solvents for years and that was all he had used the night before his death. Chloral hydrate was apparently not prescribed or otherwise available to the deceased or anyone else in the household. It was then realized that the trichloroethanol could have resulted from trichloroethylene, and the content of the glue found at the scene was investigated further. The manufacturer stated that the solvent in the glue contained 95–97% trichloroethylene. Subsequently, a targeted, quantitative assay was set up for trichloroethylene.

Experimental

Initial screen

Cardiac blood was screened for the presence of ethanol using headspace gas chromatography with flame-ionization detection (HS-GC–FID). An extended HS-GC–FID screen was also run for non-ethanol related solvents, the results of which were initially negative. Blood was screened for the presence of drugs by im-
munoassay (ELISA and Abbott TDx) for acetaminophen, salicylate benzodiazepines, barbiturates, cocaine metabolites, opiates and amphetamines. Blood was also screened by GC–mass spectrometry (MS) in combination with nitrogen-phosphorus detection (GC–NPD) and by GC with electron capture detection (ECD). A high concentration of trichloroethanol was detected by GC–ECD. No other drugs or metabolites were detected.

Solvent screen
The solvent screen was performed using an Agilent 5890II GC and 7694 headspace unit with a flame-ionization detector (FID). Separations were accomplished using a 30 m, Rtx-BAC1 capillary column (0.53-mm i.d., 3.0-µm film thickness, Restek #18001). To 0.5 mL blood or other specimen, isopentyl alcohol was added as the internal standard (10 µL in 1.0 mL 1 M ammonium sulfate) in a 20-mL headspace vial and immediately sealed. The vial was equilibrated at 60°C for 20 min prior to injection of 1.0 mL headspace. Other headspace sampler conditions were vial pressurization 18 psi for 0.4 min, loop fill 0.25 min, loop equilibration 0.10 min, inject time 0.5 min, sample valve 85°C, sample line 75°C. GC conditions: splitless mode; injector 120°C; detector 200°C; and oven 60°C for 3 min, ramped at 15°C/min to 200°C, and held for 2 min. At least one positive and one negative blood-based control were included in each run. The limit of detection for trichloroethylene under ideal conditions was estimated to be 0.5 mg/L, although it may be higher in decomposing samples (see Discussion).

Trichloroethanol quantitation
Trichloroethanol was quantitatively measured by GC–FID, using an Agilent 5890II GC. Separations were accomplished using a 10-m HP-5 capillary column (0.32-mm i.d., 1.0-µm film thickness, Agilent Technologies). To 0.5 mL blood or other specimen, ethylchlorovynol, as the internal standard (0.1 mL of a solution containing 10 µg/0.1 mL deionized water), 1 mL phosphate buffer (pH 7.4, 1 M), and 3 mL 1-chlorobutane were added and mixed for 10 min. After centrifugation for 10 min, the upper organic layer was removed and concentrated under nitrogen to about 100 µL. One microliter extract was analyzed by GC–FID with the following conditions: splitless mode; injector 260°C; detector 300°C; and oven 50°C for 0.5 min, ramped at 10°C/min to 120°C, and held for 5 min. Five blood-based calibrators ranging from 5 to 100 mg/L were prepared by adding appropriate amounts of a methanolic solution of trichloroethanol. The calibration fitted a quadratic curve with a correlation coefficient of 0.9993. An independently prepared blood-based trichloroethanol control, which read within ± 15% of the target, was also run. Trichloroethanol eluted at 3.06 min and ethylchlorovynol at 4.79 min.

Trichloroethylene quantitation
Trichloroethylene was quantitatively measured by HS-GC–FID, using an Agilent 5890II GC and 7694 headspace unit, using the similar conditions as for the solvent screen, except for the oven temperature ramp: 60°C for 1 min, ramped at 15°C/min to 150°C, and held for 1 min. To 1 mL blood or other specimen, 1,1,1-trichloroethane was added as the internal standard (30 µL of a solution containing 5 µL 1,1,1-trichloroethane in 25 mL methanol) in a 20-mL headspace vial and immediately sealed. Six blood-based calibrators ranging from 0.5 to 10 mg/L were prepared by adding appropriate amounts of a methanolic solution of trichloroethylene. A similar volume of methanol was added to case specimens and controls. The calibration curve deviated only slightly from linearity, with a correlation coefficient (quadratic fit) of 0.9999. An independently prepared blood-based trichloroethylene control, which read within ± 15% of the target, was also run. Trichloroethylene eluted at 2.57 min and 1,1,1-trichloroethane at 2.18 min.

Results and Discussion
Initial toxicology testing revealed only a blood trichloroethanol concentration of 80 mg/L. Because this was initially interpreted as being consistent with abuse or overdose of chloral hydrate, the death was certified as being due to "Trichloroethanol Toxicity". Chloral hydrate is extensively metabolized to trichloroethylene with an estimated half-life of only minutes (2,3). Chloral hydrate doses of 1000 mg generally result in blood trichloroethanol concentrations of less than 15 mg/L. In one study, five subjects receiving single doses of 1000 mg achieved blood concentrations of 2–12 mg (average 8.0 mg/L) after 1 h (4). Conversely, blood trichloroethylene concentrations of 20–240 mg/L (average 119 mg/L) have been reported in a series of 14 deaths attributed to chloral hydrate (5).
In our case, four months after the death occurred, after hearing that the family of the deceased insisted that he did not have access to chloral hydrate and that he had only been abusing commercial glue, we received further information that the solvent in the can of glue contained trichloroethylene. We subsequently ran a targeted assay with the following results: trichloroethylene at 1.1 mg/L in cardiac blood, 4.5 mg/L in bile, and 2.5 mg/kg in liver.
However, trichloroethylene is extensively metabolized, the primary urinary metabolites being trichloroethanol and trichloroacetic acid, plus conjugates (1). One study indicated that about 45% of a dose of trichloroethylene is excreted into the urine as trichloroethanol glucuronide (6). Later studies indicated chloral hydrate may be a transient metabolite of trichloroethylene (7). Szlatenyi and Wang (8) reported the case of a man who developed toxicity after intentionally inhaling trichloroethylene; his serum trichloroethylene concentration was 119 mg/L on admission to hospital and his urine trichloroethanol was 51 mg/L. The concentrations of trichloroethylene were not measured (8). De Baere et al. (9) reported a fatality where a male who died after an apparent oral ingestion of trichloroethylene with a blood concentration of 210 mg/L; trichloroethanol was not measured in blood, although it was measured in the liver, kidney, and lungs (15.7, 78.7, and 4.0 mg/kg, respectively). Conversely, another report of a man who intentionally overdosed on 70 mL liquid trichloroethylene developed a maximal blood concentration of only 4.1 mg/L (trichloroethanol was not measured) (10). Coopman et al. (11) reported the accidental inhalation death of a man coating the wall of an enclosed room with a material
containing trichloroethylene; the subclavian blood concentration of trichloroethylene was 84 mg/L and in femoral blood 40 mg/L; trichloroethanol was not tested for (11). Several other deaths attributed to trichloroethylene overdose have had blood trichloroethylene concentrations ranging from 3 to 110 mg/L (average 27) (12).

In our case, it would have been anticipated that the trichloroethylene concentrations measured would have been significantly lower than they were at the time of autopsy, given the period of four months between original receipt and quantitative analysis, with storage at refrigeration temperature of 4–6°C. The original screen for solvents and the trichloroethanol and the trichloroethylene quantitations were all performed on aliquots of a cardiac blood sample (40 mL supplied in a 80-mL capacity screw-capped urine-style container). But even though the original solvent screen was not directed towards trichloroethylene, retrospective review of the case data indicates a small GC peak with a relative retention time very close to that expected. Comparison of the relative peak areas of the trichloroethylene and solvent screen internal standard (isopentyl alcohol), indicates an amount of the same order of magnitude as the subsequent quantitative assay (i.e., about 1 mg/L). Also, given the bulk of the liver sample (approximately 50 g) and the relative consistency of the blood, bile, and liver concentrations, it is likely that the original trichloroethylene concentrations were in the lower end of the range found in the cases summarized by Baselt (12). Certainly, the small peak seen in the original screen was not significantly bigger than the various unidentified peaks often seen in postmortem blood samples, accounting for our failure to identify it initially. Ideally, blood and tissue samples from suspect volatile substance abuse (VSA) cases should be collected into glass containers with solvent impermeable caps (e.g., Teflon lined) and filled to minimize headspace losses. However, as in many sudden death investigations, either the facts of the VSA death are not fully appreciated at the time of autopsy, or appropriate containers not readily available at the time samples are collected.

Initially puzzling was why the trichloroethylene concentration in our case was so low (even allowing for the fact that there was some loss due to its volatility), but that the trichloroethanol concentration was more than 50-fold higher. Review of the literature shows that the published half-lives of trichloroethylene and trichloroethanol are 30–40 h and 6–10 h, respectively (12), which is the reverse of what would be expected given the apparent accumulation of trichloroethanol. However, apparent half-lives can be misleading. The commonly published trichloroethylene half-life of 30–40 h is fact the biological half-life, estimated through urinary excretion studies, and reflects the length of time for the body to rid itself of half the burden of trichloroethylene. That is very different from the short half-life in blood that would be expected as trichloroethylene is redistributed from blood to fatty tissue throughout the body following acute exposure, analogous to the short distribution half-life in blood of halogenated anesthetics. However, the half-life usually cited for the considerably more polar metabolite, trichloroethanol, is the half-life in blood, not the longer biological half-life. Therefore, in an individual chronically abusing trichloroethylene, accumulation in the blood would not be expected because it is being rapidly cleared to fatty tissue throughout the body, whereas clearance of the more polar metabolite trichloroethanol would not be as rapid because it depends more on the slower processes of metabolism and excretion through the kidneys. This is consistent with the literature reports of trichloroethylene exposure where chronic exposure results in relatively low blood concentrations, but where the relatively high blood concentrations reported have resulted from acute exposure to very large amounts, often via oral ingestion (9,10).

Although the high blood trichloroethanol concentrations in this case almost certainly resulted from trichloroethylene abuse, the metabolite, trichloroethanol, very likely played an important role in the mechanism of death. The concentrations are well into the range previously reported for chloral hydrate caused fatalities and are high enough to produce CNS depression and possibly cardiac toxicity. Therefore, although the source of trichloroethanol in this case is now known to be trichloroethylene abuse, the recorded cause of death of “Trichloroethanol Toxicity” may still be justified. Trichloroethene and other solvents are known to cause very sudden cardiac and/or respiratory arrest during acute episodes of inhalation of high concentrations, especially in a manner that causes a reduced intake of fresh air (13,14). In our case, although a sudden death during or immediately after an acute episode of abuse is possible, it is unlikely because the individual was found dead in bed in the morning, with no nearby evidence of the source of solvent.

Conclusions

Toxicologists should be mindful of the fact that high concentrations of trichloroethanol can result from trichloroethylene abuse, as well as from chloral hydrate ingestion.

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Manuscript received July 13, 2007;
revision received August 7, 2007.