Elevated CPK levels after hydrazine inhalation exposure in an F16 aircraft technician

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ABSTRACT

Hydrazine is a hazardous material that is commonly used in the pharmaceutical industry, as well as in rocket and jet fuels, including the emergency power unit of F-16 model jets. We present four ground crew technicians who were exposed to hydrazine for less than one minute, due to a voltage fall in an F-16 jet. Physical examinations were normal and none of the technicians were symptomatic for toxicity. One of the technicians had abnormal blood chemistry levels for liver and muscle enzymes: serum glutamic-oxaloacetic transaminase (SGOT)-321U/L, serum glutamate-pyruvate transaminase (SGPT)-123U/L, and creatine phosphokinase (CPK) 3300U/L. The CPK level peaked during hospitalization to 20960U/L at 36 h after the exposure, and subsequently declined. Upon release from the hospital, 48 h after the exposure, the CPK level was 9429U/L. In repeated tests one week and one year after exposure, liver function and CPK levels were normal. We conclude that evaluation of blood tests is important, in addition to a physical examination, in asymptomatic persons following exposure to even short term highly elevated levels of hydrazine.

1. Introduction

Hydrazine, formula N₂H₄, is a colorless flammable organic compound, with an odor resembling ammonia and a boiling point of 113.5 Celcius. Hydrazine appears naturally in tobacco products, such as cigarette smoke [1]; and is widely used in the organic pharmaceutical industry, such as in the production of isoniazide, allopurinol, and fluconazole [2]; in-organic synthesis, as a foaming agent in the production of polymers and Liquid Crystal Display (LCD) screens, as a corrosion retardant in electric and nuclear power plants, and in rocket and jet fuel cells [3]. Currently, 70% hydrazine hydration (H-70) is used with iridium to propel a gas turbine in the emergency power unit (EPU) of various F-16 models; the hydraulic systems support the space shuttle [1].

Hydrazine is a hazardous material, with IHLH (immediately dangerous to life or health) of 50 ppm, the odor threshold is 0.3–5 ppm (IDLH for ammonia is 15 ppm). A number of guidelines exist regarding human exposure limits [4]. Humans with either acute or chronic hydrazine exposure are at increased risk of developing serious health complications including immediate neuropsychological, respiratory and dermatological reactions, and cancer, in the long term [5]. Hepatic changes due to hydrazine inhalation have been demonstrated in animal studies [6]. Only a small number of human cases of hepatoxicity due to hydrazine inhalation have been published [4–6]. We report a case of significantly elevated CPK levels following brief hydrazine vapor inhalation in a healthy young man, which resolved completely.

2. Case report

In February 2011, while operating an F-16 aircraft inside an underground hangar, a voltage fall occurred. As a result, the plane's EPU entered into operation. The hangar dome space filled with hydrazine vapor. Four ground crew technicians in their twenties, previously healthy, were in the hangar and inhaled the hydrazine fumes. None of them was exposed to hydrazine in the past. They were between three to five meters away from the EPU exhaust. Two fighter pilots were on the plane with a closed canopy and did not inhale the hydrazine fumes. None of them was exposed to hydrazine in the past. They were between three to five meters away from the EPU exhaust. Two fighter pilots were on the plane with a closed canopy and did not inhale the hydrazine fumes. All the technicians wore plain clothes without masks. The ground crew left the hangar and the plane took off. The exposure time was less than one minute. The ambient temperature was estimated to be around 10 °C.

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The concentration of hydrazine vapor at the affected hangar was not measured, but visible vapors took some time to dissipate with the plane’s jet exhaust fanning the flames.

Immediately after exposure, all exposed personnel were examined by a flight surgeon for signs of neurological, pulmonary, or other injury. All were asymptomatic and initial physical examinations were all normal.

As by Israeli air force regulations, all exposed personnel performed spirometry, blood and urine tests. All the spirometry tests were decoded as normal. The laboratory tests showed that one of the ground technicians, a 21 years old male, previously healthy, had abnormal blood chemistry levels for liver and muscle enzymes: SGOT-321, SGPT-123, and creatine phosphokinase (CPK) 3300U/L. The technician was summoned for an additional examination. He denied any background of physical exertion including sport, exposure to fever, toxic substances or medications. A repeat physical examination was again normal.

The technician was treated with intravenous fluids and transported to an emergency room at a tertiary-level medical center. No evidence of neurological or pulmonary abnormality was detected on physical examination.12-lead Electrocardiography showed normal sinus rhythm. Repeated blood tests demonstrated normal complete blood count, and increased enzyme levels to: SGOT-3215, SGPT-1234, CPK 20960U/L (Table 1). Blood glucose was normal at 92 mg/dl, and creatine was 0.4 mg/L. There was no neurological or pulmonary abnormality was detected on physical examination. No evidence of neurological, pulmonary or other injury. All were asymptomatic and initial physical examinations were all normal.

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The technician remained in the hospital under supervision and was treated with crystalloid intravenous fluids only. The CPK level peaked during hospitalization to 20960U/L 36 h after the exposure and then started to decline. Upon his release from the hospital, 48 h later, the CPK level decreased to 9429U/L. In repeated tests one week and one year after exposure, liver function and CPK levels were normal. The technician continued his military service in good health.

### Table 1

| Normal range       | Day 1 | Day 2 | Day 3 | Day 4 | Day 21 |
|--------------------|-------|-------|-------|-------|--------|
| SGPT (ALT)         | 7-55 U/L | 123   | 145   | 134   | 115    | 34.2   |
| SGPT (AST)         | 8-48 U/L | 321   | 378   | 204   | 152    | 19.3   |
| CPK                | 52 - 336 U/L | 3394 | 20,960 | 12156 | 9429   | 109.9  |


3. Discussion

We report short, under one minute, exposure to hydrazine that resulted in very highly elevated levels of liver and muscle enzymes in a man who did not have any symptoms of toxicity. The enzyme levels decreased substantially during 48 h of treatment with intravenous fluids, and subsequently normalized. We documented a reduction of 42% in the CPK level from day two to day three, and 23% reduction from day three to day four.

Only a few cases of hydrazine toxicity have been described in the literature. Sotaniemi et al. described a fatal case of hydrazine inhalation toxicity in which the patient developed liver degeneration and necrosis [7]. In vitro studies performed on rat hepatocytes suggest that the acute cytotoxicity caused by hydrazine is primarily mediated through the induction of oxidative stress, due to increased generation of reactive oxygen species and the depletion of reduced glutathione [6].

Hydrazine vapor is readily absorbed through the lungs. The Occupational Safety and Health Administration determined an exposure limit for hydrazine of 1 ppm (1.3 mg/m3), as a time-weighted average concentration over 8 h. The National Institute for Occupational Safety and Health recommends an exposure limit of 0.03 ppm (0.04 mg/m3) as a ceiling concentration for 2 h [1].

In this report, we described a significant increase in CPK levels (up to 20,960 U/L) without respiratory signs, although the exposure to hydrazine was inhalation exposure. Presumably, the response to hydrazine of one technician only, could be due to a predisposition at the cellular or mitochondrial level, though this cannot be proved.

We recommend that all physicians treating people exposed to hydrazine, in industry, the air force or the navy, be aware of the diversity in symptoms, and consider the possibility of significant poisoning also in asymptomatic patients.

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