Toxicity in man due to stain removers containing 1,2-dichloropropane

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ABSTRACT There are reports that 1,2-dichloropropane, a constituent of many commercial solvents and stain removers in Italy, has caused severe liver damage and, sometimes, acute renal failure. Between 1980 and 1983 three cases of 1,2-dichloropropane intoxication (1 by ingestion, 2 by inhalation) were observed. Clinical features included severe liver damage, acute renal failure (2 patients), haemolytic anaemia, and disseminated intravascular coagulation. The most surprising features were haemolytic anaemia and disseminated intravascular coagulation which have not been reported before. The clinical picture was similar despite different modes of exposure.

1,2-Dichloropropane (1,2-D), or propylene dichloride ($\text{CH}_2\text{Cl}.\text{CHCl}.\text{CH}_3$), is a colourless and volatile (vapour pressure 35 mm Hg at 70°F) liquid widely used in commercial solvents and stain removers. Its toxicity in animals has been known since 1946,¹ whereas in man it was reported for the first time only in 1968 when liver damage was found in six patients, one of whom had acute renal failure.²⁻⁴ In these cases 1,2-D was ingested. More recently, Parker and his coworkers⁵ studied the toxicity of 1,2-D by inhalation in mice and rats and concluded that only lethal concentrations can produce appreciable injury to the lung, liver, and kidney, whereas multiple sublethal exposure resulted only in slight toxic effects.

Since 1,2-D is a good solvent, less expensive than other chlorinated compounds, it is widely used in Italy, even at high concentrations, in manufacturing different makes of commercial solvents and Trielina (a commercial preparation used to remove stains from clothes). A study carried out in Italy⁶ showed that in all commercial stain removers sold for domestic use 1,2-D was present at high concentrations (70-98%). Moreover, the industrial use of 1,2-D has also increased, especially in the paint industry. The increase in its domestic and industrial use and Trielina sniffing by young people⁷⁻¹⁰ has increased the risk of toxic exposure to 1,2-D.

We describe three cases of intoxication with acute hepatic, haematological, and renal (2 patients) damage caused by inhaling or ingesting 1,2-D. One

case has been previously reported.¹¹

Gas chromatographic examination of Trielina in case 1 showed almost only 1,2-D, and in case 2 showed 98% of 1,2-D (the remaining 2% was trichloroethylene and dichloroethane); in case 3 gas chromatographic examination of the solvent showed 60% of 1,2-D (the remaining 40% consisted of acetone, isobutyl alcohol, and n-butyl acetate).

Case 1

A 28 year old man admitted to hospital in April 1980 a few hours after the accidental ingestion of a stain remover sold as Trielina. On admission haemoglobin, haematocrit, renal and liver function, and coagulation test results were normal. Two days later he developed renal failure (serum creatinine 380.12 $\mu\text{mol/l}$ (4.3 mg/100 ml), creatinine clearance 20 ml/min blood urea nitrogen 7.13 mmol/l (43 mg/100 ml)), and liver damage (total bilirubin 63.27 $\mu\text{mol/l}$ (3.70 mg%) of which 41.04 (2.40) was conjugated, AST 1850 U/l, ALT 2300 U/l, prothrombin activity 25% of normal control). Slight disseminated intravascular coagulation was also found (fibrinogen degradation products 10-40 $\mu\text{g/ml}$, plasma fibrinogen 196 mg/100 ml). Forced diuresis was carried out, after which renal function improved: on the fourth day serum creatinine concentration was 155.28 $\mu\text{mol/l}$ (1.70%) and creatinine clearance 110 ml/min; liver damage persisted (total bilirubin 280.44 $\mu\text{mol/l}$ (3.70 mg/100 ml) of which 186.39 (2.40) was conjugated, AST 1510 U/l, ALT 1880 U/l, prothrombin activity 44% of normal control, and increased hepatic LDH

isoenzymes), and haemolytic anaemia appeared HCT 34.6%, unconjugated bilirubin 90.63 $\mu\text{mol/l}$ (5.3 mg/100 ml). On the seventh day the patient died of septic shock.

Case 2

A 20 year old girl complained of vomiting, abdominal pain, widespread ecchymoses, haematuria, and metrorrhagia in February 1982. A week later the symptoms regressed, and laboratory findings showed: total bilirubin 89.43 $\mu\text{mol/l}$ (5.23 mg/100 ml) of which 25.99 (1.52) was conjugated, AST 96 U/l, ALT 804 U/l, and HbsAg negative. No further clinical investigations were performed.

In November 1982 she was admitted with oliguria, epistaxis, haematuria, metrorrhagia, and periorbital and conjunctival haemorrhages. Two days before admission she had vomited and had had abdominal pain, followed by fever, with facial oedema and erythema. Laboratory findings showed severe renal failure (serum creatinine 743.4 $\mu\text{mol/l}$ (8.4 mg/100 ml), BUN 34.19 mmol/l (206 mg/100 ml)), acute liver damage (AST 660 U/l, ALT 1730 U/l, total bilirubin 193.23 $\mu\text{mol/l}$ (11.30 mg/100 ml) of which 109.44 (6.40) was conjugated, prothrombin activity 16% of normal control), haemolytic anaemia (HCT 21.6%, plasma haptoglobin undetectable), and disseminated intravascular coagulation (platelet count 10 000/mm³, fibrinogen degradation products over 40 $\mu\text{mol/ml}$, plasma fibrinogen 100 mg/100 ml, partial thromboplastin time 44 sec). C3 serum concentration was decreased (28 mg/100 ml) and C4 was undetectable in serum. A peripheral blood smear did not show fragmented red cells. The Coombs test, A and B hepatitis markers, antinuclear antibodies, and Widal-Wright and leptospira test results were negative. The patient was treated with transfusions of fresh blood (500–1200 ml for two consecutive days) and plasma (450–1200 ml a day for seven days), and underwent four haemodiafiltration sessions. Oligoanuria reversed after eight days. Renal biopsy findings were consistent with acute tubular necrosis. Three weeks after admission the patient was discharged with complete recovery of her renal and liver function and normal coagulation tests. Serum C3, C4, and haptoglobin concentrations were normal.

After much questioning the patient admitted that since January 1982 she had been sniffing Trielina every night before sleeping to sedate herself and evade reality. In fact she considered Trielina as effective as other stupeficients, cheap, and easily available. After the first acute episode in February she stopped sniffing but started again in November. During the course of one night she repeated the operation four times: the symptoms of the second episode appeared

the next morning.

Case 3

A 55 year old woman suffering from membrano-proliferative glomerulonephritis and on home haemodialysis three times a week since March 1980 was admitted in April 1983 with abdominal pain. Laboratory tests showed severe liver failure (AST and ALT over 6000 U/l, LDH about $\times 12000$ U/l, increased hepatic fractions 4 and 5 and prothrombin activity 32% of normal control). Haemolytic anaemia was also found, shown by decreased plasma haptoglobin, increased erythrocytic LDH isoenzymes, increased unconjugated bilirubin 51.3 $\mu\text{mol/l}$ (3 mg/100 ml), total bilirubin 61.56 $\mu\text{mol/l}$ (3.6 mg/100 ml), and reticulocytosis (3.4%). Haematocrit remained at the previous low level (22%). The osmotic resistance of the red cells was reduced, with 23% haemolysis at 0.60 NaCl concentration (normal values 0.5–2%). Slight disseminated intravascular coagulation was also found (platelet count 74 000/mm³, fibrinogen degradation products over 40 $\mu\text{g/ml}$, plasma fibrinogen 202 mg/100 ml). We did not perform blood transfusion and haemodialysis was continued. The patient's condition rapidly improved. A week after admission haemolytic activity disappeared (serum haptoglobin 195 mg/100 ml, erythrocytic LDH isoenzymes decreased, total bilirubin 14.70 $\mu\text{mol/l}$ (0.86 mg%)) as did the disseminated intravascular coagulation (platelet count 151 000/mm³, fibrinogen degradation products less than 10 $\mu\text{g/ml}$, plasma fibrinogen 310 mg/100 ml). The osmotic resistance returned to normal and the liver disease improved (AST 49 U/l, ALT 736 U/l, LDH 500 U/l, prothrombin activity 100% of normal control). HbsAg and Widal-Wright test results were negative. Peripheral blood smear did not show fragmented red cells. Biliary and liver echography did not show pathological findings.

The patient disclosed that three days before admission she had spent six hours cleaning her flat using two litres of solvent, during which time she noticed no untoward effects, only a nasty smell. In the afternoon she underwent haemodialysis at home. During the following three days she developed anorexia, abdominal pain, and nocturnal sweating, and was admitted to hospital.

Discussion

Organic solvent toxicity has been known for many years. Renal and hepatic damage has been described after exposure to some chlorinated aliphatic hydrocarbons^{2,7,8,12,13}; 1,2-D toxicity in man is less

often reported.²⁴ In the three cases reported here 1,2-D apparently caused renal and hepatic damage, a haemolytic anaemia, and disseminated intravascular coagulation.

Renal damage—Two patients (1 and 2) had normal renal function before exposure to 1,2-D; patient 3 was on haemodialysis. Though patient 1 did not undergo renal biopsy the laboratory data and clinical course were consistent with acute tubular necrosis. Renal biopsy was performed on patient 2, and histological examination showed acute tubular necrosis. Immunofluorescence and electron microscopy investigations were negative. This is consistent with a direct toxic damage on the renal tubular cells, as suggested by experimental studies.^{15,13}

Hepatic damage—All three patients showed impairment of liver function. None underwent liver biopsy, but we may presume the presence of centrilobular hepatic necrosis, as observed by some authors in experimental¹ and clinical^{4,8} studies. It is interesting that LDH-isoenzymes electrophoresis, performed in patients 1 and 3, showed not only increased hepatic fractions 4 and 5 but also fraction 6 which is usually present only in the spermatid fluid; this fraction disappeared after the recovery of hepatic function.

Haemolytic anaemia—Haemolytic anaemia in 1,2-D intoxication has never been reported either in experimental studies or in man but was present in our patients. The Coombs test results were negative, peripheral smear showed no fragmented red cells, and osmotic resistance was reduced (case 3). We think that a direct toxic effect on red blood cells is responsible for the haemolysis.

Disseminated intravascular coagulation, previously unreported, was observed in each of the three patients but was clinically important only in patient 2.

In conclusion, our patients had acute renal and hepatic injury, haemolytic anaemia, and disseminated intravascular coagulation resulting from exposure to 1,2-D. The clinical picture was similar in all three patients, despite different modes of exposure: ingestion or inhalation. In all cases an interval of more than 24 hours elapsed between exposure to 1,2-D and the onset of symptoms. Since 80–90% of 1,2-D and its

metabolites are eliminated in the expired air, urine, and faeces within 24 hours after exposure,^{5,14,15} we may conclude that when the symptoms appear the analysis of blood, urine, and faeces for the solvent is useless. The wide use of 1,2-D in commercial solvents and Trielina could be a dangerous and unknown source of intoxication because they are commonly found in the home and are sniffed by young people. For this reason greater knowledge about chronic toxicity and more suitable legal measures concerning the use of 1,2-D are required.

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