CASE REPORT

Rhabdomyolysis with acute tubular necrosis following occupational inhalation of thinners

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Abstract
Thinners are mixtures of organic solvents commonly containing toluene, xylene, acetone, hexane, benzene and methyl isobutyl ketone. This report describes a case of rhabdomyolysis with acute tubular necrosis and renal failure, most likely attributable to toluene, following occupational exposure to thinners while cleaning a steel water tank. These adverse health effects have previously been reported following acute poisoning or intentional inhalation by drug abusers, but rarely in the occupational setting. Poor working conditions, lack of health and safety training and delayed treatment contributed to the onset and severity of the patient’s complications. This case emphasizes the need for strict control measures, including adequate ventilation, training on working in confined spaces, appropriate personal protective equipment and emergency rescue procedures in such settings. In addition, rhabdomyolysis, acute tubular necrosis and renal failure should be added to safety data material as possible complications of excessive inhalation of thinners.

Key words
Acute tubular necrosis; confined space; renal failure; rhabdomyolysis; thinners; toluene.

Introduction

Thinners are an organic solvent mixture of aromatic hydrocarbons, halogenated hydrocarbons and naphtha, most commonly toluene, xylene, acetone, hexane, benzene and methyl isobutyl ketone [1–3]. Composition varies significantly depending on local regulatory specifications and manufacturing processes [1]. Adverse effects of exposure have been reported following acute poisoning or intentional inhalation by drug abusers. Cardiac, renal, neurological and hepatic complications are known chronic effects of exposure [2]. We describe a case of rhabdomyolysis with acute tubular necrosis and renal failure following thinners inhalation while cleaning a steel tank.

Case report

A 42-year-old patient attended the occupational medicine clinic, Groote Schuur Hospital, Cape Town, South Africa in January 2016. He was a worker at a boiler-making company and was exposed to thinners while repairing and cleaning a 4000 L steel water tank at an offsite location with a co-worker. This involved grinding the inner surface of the tank and cleaning the surface with thinners. During this activity, both workers became unwell, with headache, body pains and weakness rendering them temporarily immobile. They could not summon help as they were in a basement with no outside contact. This was their first such work and they denied receiving any safety training. They did not use personal protective equipment (PPE) and the oxygen cylinder provided was found to be empty during attempted use. They received assistance after 1½ h and were taken to the employer site. While the co-worker had recovered from the incident, the patient was still unsteady on his feet. He received no medical attention and was instead taken home. With a neighbour’s assistance, he was admitted to a local hospital that evening, discharged after 2 days but readmitted on the fourth day post-incident before being transferred to a tertiary hospital.

On admission to the tertiary hospital, abnormal clinical findings were oliguria, raised systolic blood pressure (151/53 mm Hg) and mild generalized abdominal tenderness. Serum creatinine was elevated [1134 µmol/L (laboratory range 64–104)] as was serum urea [31.7 mmol/L (2.1–7.1)], with normal pH and normal serum sodium and potassium. Serum creatinine kinase was greatly elevated [166815 U/L (20–200)] as were alanine aminotransferase [1357 U/L (10–40)] and aspartate aminotransferase [2056 U/L (15–40)]. Abdominal ultrasound showed bilateral hyperechoic kidneys consistent
with acute kidney injury, and renal biopsy confirmed acute tubular necrosis. He was haemodialysed for 7 days with gradual improvement of renal, hepatic and muscle indices and urine output and discharged after 4 weeks. He has since been clinically stable with creatinine and urea having normalized at 87 µmol/L and 6.1 mmol/L, respectively, although his creatinine kinase has remained elevated at 3225 U/L, and further investigation at a rheumatology clinic is pending.

The employer was initially uncooperative, insisting that the patient was an 'independent contractor' rather than an employee. The employee elected not to resume his relationship with the employer. A worker’s compensation claim was eventually submitted and is currently pending.

**Discussion**

This report describes a case of short-term occupational exposure to thinners at a presumed high concentration in a confined space, leading to rhabdomyolysis, acute tubular necrosis and renal failure. A similar case of occupational thinner intoxication with rhabdomyolysis has previously been described in a painter [4]. Of the mixture of solvents used here (Table 1), only toluene has been reported to cause these effects, including fatal outcomes [5]. Toluene is lipid soluble, hence readily absorbed from the respiratory and gastrointestinal tracts and skin [6]. Inhalation is likely to have been the primary source of exposure. Hypokalemia has been described as underlying a number of the features of acute toluene intoxication, including muscle weakness and rhabdomyolysis [5]. While our patient’s blood results showed no hypokalemia or acidosis, we were unable to retrieve records of his immediate post-incident admission and the presence of these at the time of the incident cannot be ruled out [5]. In addition to direct muscle injury, prolonged immobilization after intoxication may itself contribute to rhabdomyolysis, as a result of tissue compression, increasing the risk of muscle ischaemia and subsequent rhabdomyolysis [7].

Both glomerular and tubular renal damage have been described in acute toluene poisoning [5]. In this case, acute tubular necrosis was confirmed by biopsy. Rhabdomyolysis, vomiting, dehydration and tubular injury may all contribute to acute renal failure [5]. In animal studies, exposure to high concentrations of toluene has been shown to cause renal tubular necrosis with tubular casts [6]. Early aggressive fluid replacement to restore renal blood flow and increase excretion of nephrotoxic compounds is crucial when treating rhabdomyolysis in order to prevent complications [7]. Toluene may also produce acute hepatic effects, consistent with the transient transaminase elevation noted in our patient [5,8].

Hazardous working conditions, lack of adequate health and safety control measures including training, lack of compliance with health and safety requirements and delayed treatment, as described above, all contributed to the onset and severity of the kidney injury in this case. The strict requirements for a safe system of work in confined spaces are well established [9] and, in South Africa, are governed by general safety regulations [10]. Furthermore, the safety data sheet for the specific thinners used recommended adequate ventilation and use of appropriate respiratory protection when working with the product.

This case confirms the risk associated with work in confined spaces and also identifies a hazard that has not been well described, namely, acute muscle injury with renal failure following the occupational inhalation of thinners. Basic protective measures should include use of thinners of low toxicity, prior risk assessment and, if necessary, augmentation of ventilation, worker training on inhalational hazards, provision of appropriate PPE and anticipation of thermal stress increasing exposure and risk of dehydration. Emergency rescue arrangements should include pre-checking equipment such as rescue air or oxygen cylinders, avoiding free discharge of cylinders in the confined space, having at least one person trained in resuscitation outside the confined space and rapid access to medical care. Finally, rhabdomyolysis, acute tubular necrosis and renal failure should be included in safety data material as possible complications of thinner inhalation.

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Concentration</th>
</tr>
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<tbody>
<tr>
<td>Xylene, mixed isomers</td>
<td>&lt;45 %W</td>
</tr>
<tr>
<td>Ethylbenzene</td>
<td>&lt;15 %W</td>
</tr>
<tr>
<td>Toluene</td>
<td>&lt;40 %W</td>
</tr>
<tr>
<td>Naphtha (petroleum), hydrotreated light</td>
<td>&lt;35 %W</td>
</tr>
</tbody>
</table>

%W: percentage composition by weight.

**Key points**

- Occupational inhalational thinner exposure of sufficient intensity may result in rhabdomyolysis, acute tubular necrosis and renal failure. Toluene is the likely causative agent in the case reported.
- Protective measures for work involving the use of such substances in confined spaces include prior risk assessment, use of low toxicity chemical products, adequate ventilation, safety training, appropriate personal protective equipment and emergency rescue procedures.
- Early medical treatment in the event of toxic exposure to such substances is crucial. Rhabdomyolysis, acute tubular necrosis and renal failure should be included in safety data material as complications of excessive thinner inhalation.
**Acknowledgement**

Richard Whittaker provided valuable information on the appropriate safety procedures for such settings.

**Conflicts of interest**

None declared.

**References**