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Acute Arsenic Poisoning in Two Siblings

Melisa W. Lai, MD*‡§; Edward W. Boyer, MD, PhD*§; Monica E. Kleinman, MD§#; Nancy M. Rodig, MD**; and Michele Burns Ewald, MD*‡§

ABSTRACT. We report a case series of acute arsenic poisoning of 2 siblings, a 4-month-old male infant and his 2-year-old sister. Each child ingested solubilized inorganic arsenic from an outdated pesticide that was misidentified as spring water. The 4-month-old child ingested a dose of arsenic that was lethal despite extraordinary attempts at arsenic removal, including chelation therapy, extracorporeal membrane oxygenation, exchange transfusion, and hemodialysis. The 2-year-old fared well with conventional therapy. Pediatrics 2005; 116:249–257; arsenic, poisoning, toxicokinetics, pharmacokinetics, British anti-lesiwse, dimercaprol, succimer, DMSA, DMPS, chelation therapy, extracorporeal membrane oxygenation, ECMO, exchange transfusion, hemodialysis, heavy metal poisoning, survival, pediatric lethal dose.

ABBREVIATIONS. DMSA, 2,3-dimercaptosuccinic acid; DMPS, 2,3-dimercaptop-1-propanesulfonate; BAL, British anti-lesiwse; ECMO, extracorporeal membrane oxygenation.

Arsenic is a heavy metal that is odorless, colorless, and tasteless in solubilized form. It is ubiquitous throughout our environment at low background levels and is used most commonly in mining operations (for smelting), in the agricultural field (as an herbicide and pesticide, although not for food crops in the United States), and in the electronics industry (for semiconductors and lasers).

Inorganic arsenic is a highly toxic transition metal; poisoning from this metal has been treated primarily with supportive care and antidote administration. Children in the United States are unlikely to ingest significant amounts from concentrated sources, and clinically significant dermal absorption of arsenic from “pressure-treated” wood (lumber treated with chromated copper arsenate), which has been used to build numerous playgrounds and decks, has not been demonstrated.1,2 However, accidental poisoning still occurs, and there is the potential for therapeutic dosing errors with arsenic trioxide (Trisenox [Cell Therapeutics, Seattle, WA]), which is used to treat patients with acute promyelocytic leukemia. Arsenic also still plays a role in acts of suicidal and homicidal intent.

Unfortunately, no existing therapies have been effective in massive overdoses. We describe a child who was treated successfully with conventional therapy for arsenic poisoning, as well as the use of several adjunctive therapies for an infant with life-threatening acute arsenic poisoning. These novel approaches may be useful for other patients with sublethal ingestions for whom conventional treatments are ineffective or inadequate.

CASE REPORTS

Ingestion

A 4-month-old male patient and his 2-year-old sister attended a cookout with their parents. The host provided the parents with a clear, unmarked, plastic container that contained a liquid and purportedly stored spring water (Fig 1). A drinking cup was filled for the toddler, and Enfamil with Iron (Mead Johnson Nutritional Division, Evansville, IN) was reconstituted with the liquid and given to the infant. The 4-month-old patient (patient 1) ingested between 2 and 3 fl oz of the material. The 2-year-old patient (patient 2) drank a small amount and spat it out, telling her parents that it “tasted bad.” Within 10 minutes, both children began vomiting. The parents brought their children to a local emergency department in their private vehicle. En route, patient 1 developed bloody emesis.

On arrival at the community hospital emergency department, both children were still vomiting but had normal vital signs. Notably, the emergency department staff observed that the reconstituted infant formula was purple in color. While the father retrieved the bottle of “spring water” from the cookout, supportive measures were started at the hospital, including intravenous fluid therapy for both children.

Approximately 3 hours after ingestion, both children had ceased vomiting and their father returned with the bottle that contained the liquid. A nurse found a product label that described an outdated herbicide that was 40% arsenic by volume (23.1% by weight) (Fig 2). The children were transferred to a tertiary care pediatric hospital.

Course of Patient 1

During transfer, patient 1 became comatose. On arrival, he was orotracheally intubated and central venous access was obtained. The patient was tachycardic and hypotensive despite intravenous administration of 30 mL/kg normal saline solution. A continuous infusion of dopamine was initiated, and the patient was admitted to the ICU. Standard chelation therapy with British anti-lesiwse (BAL) through intramuscular injection of 3 mg/kg every 4 hours was provided. Within 6 hours after ingestion, the pupils of patient 1 became fixed and dilated; he had no spontaneous movement despite withholding of sedation after intubation. Blood gas analysis showed severe metabolic acidosis despite treatment with sodium bicarbonate, and the patient had evidence of disseminated intravascular coagulation (Table 1).
Continuous resuscitation with intravenous crystalloid and colloidal therapy and vasoactive infusions failed to prevent cardiovascular collapse. The patient developed ventricular fibrillation and multiple ventricular nonperfusing tachyarrhythmias, devolving into torsades de pointes (Fig 3), and was treated with lidocaine hydrochloride, magnesium sulfate, bretylium tosylate, and defibrillation. Twelve hours after ingestion, the patient underwent extracorporeal membrane oxygenation (ECMO) on an emergency basis.

For a brief period after cannulation, some pupillary reactivity returned and the patient exhibited some spontaneous and nonposturing movement. He was anuric from the time of ingestion until 2 hours after initiation of ECMO, when he produced 107 mL of urine in 2.5 hours and then became anuric again. The patient had an ongoing capillary leak and became markedly edematous. He continued to receive intramuscular injections of BAL (5 mg/kg) every 4 hours for chelation. Extracorporeal elimination of arsenic through 2 runs of hemodialysis and a single-volume exchange transfusion was attempted.

Because of the failure of the preceding therapies, patient 1 received the experimental chelator 2,3-dimercapto-1-propanesulfonate (DMPS). This therapy also failed to produce clinical improvement. The patient sustained ventricular tachyarrhythmias refractory to pharmacologic and electrical conversion. Supportive measures were discontinued 36 hours after ingestion. Although the patient weighed 8 kg at admission, his weight at autopsy was 23 kg.

A spot urinary arsenic concentration had been obtained during the patient’s brief period of urine production, 14 hours after ingestion and after 2 doses of BAL; the urinary arsenic concentration was 9000 μg/L. During the patient’s first hemodialysis session, dialysis was performed with 102 L of dialysate. Dialysate toward the end of this session had an arsenic concentration of 20 μg/L, indicating a minimal arsenic removal of 2.04 mg. At autopsy, the patient’s serum arsenic concentration was 730 μg/L.

Course of Patient 2

Patient 2 was admitted to the ICU for hemodynamic monitoring. She had sinus tachycardia, with heart rates ranging from 130 to 180 beats per minute in the initial 12 hours after ingestion. She demonstrated no hypotension or arrhythmias. She received intravenous fluids at twice the maintenance rate and standard chelation therapy with BAL (5 mg/kg) through intramuscular injection every 4 hours. While in the ICU, her QTc prolonged to as long as 527 milliseconds at 22 hours after ingestion, decreasing to ~450 milliseconds without specific therapy. Her electrocardiographic results remained normal for the remainder of her hospital course. On hospital day 4, the patient was transitioned to oral chelation therapy with 2,3-dimercaptosuccinic acid (DMSA), and BAL administration was discontinued.

Serial 24-hour urinary arsenic concentrations were measured for patient 2 during hospital days 2 through 13 (Fig 4). The peak urinary arsenic concentration was 4920 μg/L from her first 24-hour collection (hours 19–43 after ingestion), quickly decreasing to 100 μg/L by the time of her discharge on hospital day 13. One week after chelation therapy was discontinued, the patient’s urinary arsenic concentration decreased to 56 μg/L. Her urinary arsenic concentration was 10 μg/L 3 weeks after chelation and was undetectable 7 weeks later. Patient 2 retained normal renal function throughout her course. She maintained a urine output of 2.6 to 5.4 mL/kg per hour. Her creatinine levels ranged from 0.2 to 0.6 mg/dL during her hospitalization. In the follow-up period, the patient had normal urine output, according to her parents, and creatinine levels were measured at 0.2 to 0.3 mg/dL. Neurologic examination results were normal except for the patient being described at presentation as less interactive than usual; within 24 hours after admission, her mental status had normalized. Subsequent neurologic examination results were normal. Patient 2 continues to be monitored by the toxicology service as an outpatient. At 1 year after ingestion, she displays no signs of arsenic-associated illness or toxicity and has met or surpassed expected developmental milestones.

Calculated Amounts of Ingested Arsenic

Aliquots of the clear liquid and reconstituted infant formula were sent to the Massachusetts State Laboratory Institute (Jamaica Plain, MA) for determination and confirmation of arsenic concentrations. The measured arsenic levels were as follows: clear liquid: 7.6% arsenic by weight; infant formula (including formula solute): 5.8% arsenic by weight. On the basis of an estimated 2 fl oz of formula ingested, patient 1 ingested (2 fl oz) × (29.57 mL/fl oz) × (1000 mg/mL) × (5.8% arsenic) = 3430 mg of arsenic. Patient 1 weighed 8 kg and thus might have ingested 428 mg/kg arsenic. Patient 2 was estimated to have ingested 2.5 mL of water after spitting out her sips, ie, (2.5 mL) × (1000 mg/mL) × (7.6% arsenic) = 190 mg of arsenic. Patient 2 weighed 13 kg and thus might have ingested 14.6 mg/kg arsenic. The minimal lethal dose of arsenic among humans has been estimated to be as low as 1.43 mg/kg.3

DISCUSSION

Pharmacokinetics of Arsenic

Arsenic exists in nontoxic and toxic forms. The nontoxic organic arsenobetaine [As(CH3)2CH2CO2] is found in trace amounts in all living matter and marine organisms. In contrast, inorganic compounds are highly toxic and are found in varying quantities throughout the earth’s crust, in either a trivalent (arsenite, As3+) or pentavalent (arsenate, As5+) oxidation state. When ingested as a water-soluble salt, inorganic arsenic in either oxidation state is absorbed rapidly from the gastrointestinal tract, with nearly 100% bioavailability; its rapid distribution from blood produces a serum half-life of only 1 hour.4 Clearance from the blood follows in 3 phases.5,6 In phase 1 (half-life: 1–2 hours), ~90% of arsenic redistributes from serum to tissues. In phase 2 (estimated half-life: 30 hours), the remaining 10% of serum arsenic redistributes to tissues (including erythro-
cytes); arsenic accumulation in erythrocytes occurs at an erythrocyte/plasma ratio of 3:1. Phase 3 (estimated half-life: 300 hours) involves redistribution of arsenic from tissues and erythrocytes to plasma, followed by renal elimination.

Arsenic undergoes renal elimination, with 46% to 68.9% of inorganic arsenic being excreted within the first 5 days of exposure. Chelation does not enhance the rate of elimination of arsenic from the body but renders the metal nontoxic by preventing the poisoning of several vital enzyme systems.

Molecular Toxicologic Features of Arsenic

Once distributed into soft tissues, arsenic penetrates cells and inhibits cellular energy production through mechanisms dependent on the element’s oxidation state. Arsenite (As$^{3+}$) binds to sulfhydryl moieties on dihydrolipoamide, preventing regeneration of the necessary Krebs cycle cofactor lipoamide (Fig 5A).

Arsenate (As$^{5+}$), which may undergo biotransformation to As$^{3+}$, is less toxic than As$^{3+}$ but also depletes cellular energy. As$^{5+}$ has the same oxidation state as and shares many chemical properties with inorganic phosphate (P$^{5+}$) and can substitute for P$^{5+}$ in ATP production. Arsenic-poisoned enzymes produce 1-arseno-3-phosphoglycerate rather than 1,3-bisphosphoglycerate. 1-Arsenio-3-phosphoglycerate hydrolyzes spontaneously, so that ATP continues to be produced. However, the arsenic-oxygen bond is significantly weaker than the phosphorus-oxygen bond, and 1-arsenio-3-phosphoglycerate hydrolysis yields dramatically less energy (Fig 5B).

Clinical Effects

Acute arsenic intoxication produces a distinctive toxidrome (Table 2). The hallmark of acute arsenic poisoning is severe hematemesis and diarrhea, followed by the abrupt onset of profound hypotension, tachycardia, cardiovascular collapse, and coma. Individuals who survive the acute phase may develop subsequent debilitating sensorimotor neuropathy, alteration in mental status, and patchy alopecia.

Acute Toxicity (0–24 Hours)

Hematemesis and diarrhea, often the sentinel signs of severe poisoning, occur within 1 to 4 hours of ingestion and may be related to a direct irritant effect of arsenic on the gastric mucosa. Gastrointestinal volume loss is compounded by profound capillary permeability produced by arsenic’s interruption of cellular energy production. Although the exact mechanism remains unknown, QTc prolongation and tachyarrhythmias, including torsades de pointes, may develop within the first 24 hours after ingestion. Cerebral edema, microhemorrhage, encephalopathy, and seizures may also arise from loss of capillary integrity. Acute renal failure is common and multifactorial in origin, resulting from interruption of cellular energy production, shock, direct toxicity to renal tubules, and tubular deposition of myoglobin.

Subacute Toxicity (24 Hours to 4 Weeks)

Subacute arsenic toxicity involves predominately the neurologic, cardiovascular, and integumentary systems. Within days to weeks after ingestion, many untreated or undiagnosed patients describe debilitating peripheral neuropathy, characterized by excruciating pain and severe motor weakness. Patients may also exhibit central nervous system depression and cognitive dysfunction (hallucinations, delirium, decreased memory, and confusion). Persistent QTc prolongation and the accompanying risk of torsades de pointes occur among patients with clinically significant body burdens of arsenic. Aldrich-Mees lines, ie, whitish transverse discoloration of the nails resulting from temporary interruption of growth.
plate activity, may occur within 40 days after acute arsenic poisoning but are rarely seen, occurring for only 5% of patients.18 Patchy alopecia appears 3 to 6 weeks after severe poisoning.

Chronic Toxicity (> 4 weeks)

Patients exposed to frequent small amounts of arsenic are subject to less severe but more insidious manifestations of toxicity. These findings have been monitored and reported numerous times since the installation of thousands of tube wells throughout Bangladesh in the 1970s. These wells became contaminated with arsenic due to its high content within the earth’s crust in this area. Multiple articles chronicle the higher rates of hyperkeratoses, hyperpigmentation, and lung and skin cancers that are seen throughout the region. Peripheral neuropathies may persist from large single acute ingestions or may develop from chronic small exposures to the metal.

Management of Acute Arsenic Poisoning

Aggressive Fluid Resuscitation and Cardiovascular Support

Fluid resuscitation remains the mainstay of initial management of arsenic poisoning.19 Because arsenic and its chelators are excreted principally in the urine, the kidneys are at risk of acute renal failure. The mortality rate from acute arsenic poisoning is higher than that from most poisonings because of the characteristics of the metal—how long it takes to act, how easily it is absorbed, and how toxic it is to the kidneys.

Twelve hours after ingestion, the patient’s deterioration accelerated precipitously. Thirteen hours after ingestion, the patient was receiving ECMO for cardiovascular support. He died 36 hours after ingestion. AST indicates aspartate aminotransferase; ALT, alanine aminotransferase; GGTP, γ-glutamyl transpeptidase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; MCV, mean cell volume; WBC, white blood cell; CPK, creatine phosphokinase; CK-MB, creatinine kinase, muscle and brain; ABG, arterial blood gas; PT, prothrombin; PTT, partial thromboplastin time; INR, international normalized ratio; —, not measured.

* Notable critical values.

![Fig 3. Rhythm strip for patient 1, showing an episode of torsades de pointes occurring ~11 hours after ingestion.](http://www.pediatrics.org)

### TABLE 1. Selected Laboratory Values of Patient 1

<table>
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<th>11.5</th>
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<td>147</td>
<td>153*</td>
<td>156*</td>
<td>164*</td>
<td>162*</td>
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<td>156*</td>
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<td>161*</td>
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<td>10*</td>
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<td>—</td>
<td>—</td>
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<td>PT, s</td>
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<td>21.1*</td>
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<td>PTT, s</td>
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<td>51.2*</td>
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<td>102.7*</td>
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<td>INR</td>
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<td>3.02*</td>
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<td>4.89*</td>
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Twelve hours after ingestion, the patient’s deterioration accelerated precipitously. Thirteen hours after ingestion, the patient was receiving ECMO for cardiovascular support. He died 36 hours after ingestion. AST indicates aspartate aminotransferase; ALT, alanine aminotransferase; GGTP, γ-glutamyl transpeptidase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; MCV, mean cell volume; WBC, white blood cell; CPK, creatine phosphokinase; CK-MB, creatinine kinase, muscle and brain; ABG, arterial blood gas; PT, prothrombin; PTT, partial thromboplastin time; INR, international normalized ratio; —, not measured.

* Notable critical values.
maintaining renal perfusion is critical. Clinicians often fail to appreciate the volume of intravenously administered fluid required for adequate resuscitation. Acutely poisoned patients develop enormous fluid deficits through gastrointestinal losses alone (vomiting and diarrhea), which can lead to hypovolemic shock. Intravascular volume depletion is aggravated by increased capillary permeability and a systemic inflammatory response syndrome-like response.\textsuperscript{14,20} The degree of capillary leak and resultant tissue edema is dramatic. As noted, patient 1 weighed 8 kg at admission; at autopsy, his weight was 23 kg.

**Chelation**

Chelating agents scavenge arsenic and bind it into a stable metal-chelate complex. Although chelators are not thought to reverse the enzymatic inhibition produced by arsenic, early chelation before confirmation of arsenic ingestion has produced increased rates of survival in small case series of acutely poisoned individuals.\textsuperscript{21–24} Unfortunately, only a limited number of chelating agents are available, and they are limited by bioavailability, binding ratios, weight-based dosing, mode of administration, and adverse effect profiles.

Dimercaprol (BAL in oil [Taylor Pharmaceuticals, San Clemente, CA]) remains the standard chelator for acute arsenical poisoning in the United States. It is estimated to bind 30 mg of arsenic for every 50 mg of BAL given.\textsuperscript{25} Because it is administered as an intramuscular injection, BAL may have unpredictable bioavailability among patients with severe shock and uncertain peripheral perfusion. As the only arsenical chelator able to cross the blood-brain barrier, BAL may offer some protection against toxicity in the central nervous system; however, concern exists that BAL could enhance arsenic redistribution to the brain and worsen central nervous system effects.\textsuperscript{26,27} BAL has significant adverse effects. The chelator causes fever and hypertension and can exacerbate fluid losses attributable to nausea and vomiting. Sterile abscesses may form at injection sites. BAL is also contraindicated for patients with glucose-6-phosphate dehydrogenase deficiency, because it may cause hemolysis, and it should not be given in cases of suspected iron toxicity, because the BAL-iron complex is itself toxic.\textsuperscript{28} Finally, BAL is lipid soluble and is constituted in peanut oil to prevent oxidation. It is therefore contraindicated for patients with peanut allergy, and it is constrained to administration only as an intramuscular injection, which impairs its distribution and effectiveness in shock states.

Succimer (DMSA, Chemet) is a water-soluble analog of BAL that can be administered orally. Pediatricians may be most familiar with its use as a chelator for childhood lead poisoning. Approximately 20% of an oral dose of succimer is absorbed from the gastrointestinal tract, with nearly all absorbed DMSA being available to chelate metal in a 1:1 ratio.\textsuperscript{29} DMSA had effectiveness comparable to that of BAL in decreasing arsenic concentrations in mouse livers, kidneys, brains, and spleens.\textsuperscript{30} No standardized protocol for DMSA administration in arsenic poisoning exists; current dosing guidelines are extrapolated from methods for lead chelation. Described adverse effects of DMSA include transient increases in transaminase levels, nausea and vomiting, rash, thrombocytosis, paresthesias, and pruritus.

DMPS (Unithiol) is a water-soluble analog of BAL that can be administered orally, intravenously, or intramuscularly. Developed in the former Soviet Union in the 1950s, DMPS is not approved by the Food and Drug Administration but has been used successfully in Europe for arsenic chelation.\textsuperscript{23,31,32} In the United States, DMPS was used for the mass arsenic poisonings in New Sweden, Maine, in April 2003, when the regional stocks of BAL had been exhausted. At that time, it was found to enhance

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**Fig 4.** Daily urinary arsenic excretion for patient 2. By 6 weeks after ingestion, she had no detectable arsenic in her urine.
excretion and to increase urinary arsenic concentrations, even after several days of BAL therapy. Increased urinary elimination of arsenic from DMPS may be attributable to chelation of metabolized (methylated) arsenic species. Biomethylation of As$^{3+}$ may activate or enhance arsenic toxicity. DMPS forms a complex with the first methylated species of the biomethylation sequence, monomethylarsonic acid, reducing availability for subsequent biomethylation and additional toxicity. Up to triple the urinary monomethylarsonic acid concentration was seen within 2 hours after oral administration of DMPS to patients suffering from chronic arsenic intoxication. This increase in arsenic metabolite elimination may support the effectiveness of immediate administration of DMPS in acute arsenic poisoning in the future. $d$-Penicillamine is no longer recommended for use in arsenic intoxication. It showed little efficacy in an animal model.

**Extracorporeal Elimination**

Numerous methods have been directed toward the mechanical removal or extracorporeal elimination of arsenic, including N-acetylcysteine, endoscopy, gastric irrigation with alkaline irrigant, alternative parenteral chelators, and hemodialysis. Because of arsenic’s short distribution half-life of only 1 hour, extracorporeal elimination methods are ineffective for removal of the metal once it is distributed to the tissues, and the metal-chelate complex may be of too great a mass for hemodialysis or hemofiltration. Children, however, may be better candidates for extracorporeal elimination methods, because they retain less arsenic in soft tissues than do adults.

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**Fig 5.** A indicates the mechanism of trivalent arsenic toxicity. Pyruvate is converted to acetyl-CoA through the pyruvate dehydrogenase complex (box). Lipoamide is a necessary cofactor for this conversion. Dihydrolipoamide is recycled normally to lipoamide by dihydrolipoamide dehydrogenase. Arsenite (As$^{3+}$) interrupts these biochemical processes by binding to the sulphydryl moieties on dihydrolipoamide, preventing regeneration of lipoamide and thus preventing acetyl-CoA production for entry into the Krebs cycle. B indicates the mechanism of pentavalent arsenic (As$^{5+}$) toxicity. As$^{5+}$ has the same oxidation state as and shares many chemical properties with P$^{5+}$. As$^{5+}$ substitutes for inorganic phosphate in ATP production. Arsenic-poisoned enzymes produce 1-arseno-3-phosphoglycerate rather than 1,3-bisphosphoglycerate. 1-Arseno-3-phosphoglycerate hydrolyzes spontaneously to 3-phosphoglycerate, so that ATP continues to be produced. However, because the arsenic-oxygen bond is significantly weaker than the phosphorus-oxygen bond, hydrolysis of 1-arseno-3-phosphoglycerate yields dramatically less energy. Therefore, synthesis of 1-arseno-3-phosphoglycerate represents ineffective cellular energy storage.
which possibly permits some reequilibration of arsenic into the vascular system. This finding correlates with a report of pediatric spontaneous excretion twice as fast as in adults. These distinctions may make extracorporeal elimination techniques more effective in the pediatric population.

The estimated arsenic burden of ~3430 mg for patient 1 could not have been eliminated through conventional chelation methods. Administration of BAL and DMSA according to standard dosing guidelines would have chelated at most 192 mg, <6% of the patient’s estimated arsenic burden, in a 24-hour period. The gravity of the condition of patient 1 dictated that adjunctive therapies be applied. Therefore, he received additional extracorporeal detoxifying treatments.

Patient 1 underwent venoarterial ECMO beginning 12 hours after ingestion, in response to refractory shock and cardiac rhythm disturbances. Because of the urgency of the situation, a saline-primed circuit with a volume of 500 mL was used. The patient’s hematocrit level decreased from 28% to 17% after cannulation and then increased to 38% with the use of packed red blood cell replacement and ultrafiltration. With an estimated blood volume of 642 mL for patient 1, these changes represented diluting and then replacing nearly one half of the patient’s total blood volume.

Once ECMO was begun, patient 1 had a return of pupillary activity and spontaneous movement, even before hemodialysis and an exchange transfusion were initiated. In addition, ECMO produced sufficient hemodynamic support to restore renal perfusion and urine output. These events suggest that ECMO may serve as a partial exchange transfusion that decreases tissue arsenic concentrations tran-
siently and may produce an improvement in organ function.

Because arsenic redistributes rapidly to tissues including erythrocytes, exchange transfusion may be beneficial in decreasing the body burden of arsenic in major intoxication. A single-volume exchange transfusion was performed for patient 1 at 28 hours after ingestion, with the goal of mobilizing arsenic from the tissues before administration of the experimental chelating agent DMPS.

Hemodialysis has been reserved traditionally for the elimination of arsenic from patients in renal failure. Patient 1 developed renal insufficiency and underwent his first hemodialysis session with 102 L of dialysate at 18 hours after ingestion, for the purpose of removing arsenic and arsenic-BAL complexes. His dialysate arsenic concentration was 20 μg/L toward the end of the dialysis session, which indicates a minimal arsenic removal of 2.04 mg (compared with his spot urinary level of 9 mg/L). This amount of arsenic elimination is consistent with reports of adults cases, in which 4-hour hemodialysis sessions removed 2.9 to 4.68 mg of arsenic. Arsenic’s large volume of distribution (3.3–4 L/kg) and the small amount of arsenic removed through hemodialysis suggest that arsenic is redistributed to tissues too rapidly, with too small a serum concentration gradient, for effective removal through hemodialysis. It is notable that although BAL does not impede arsenic removal through dialysis, the DMPS-arsenic complex may not be as readily dialyzable. Hemodialysis may be useful only to treat the electrolyte and fluid imbalances of renal failure and is unlikely to be helpful for removal of arsenic or arsenic-chelator complexes.

Elimination of the DMPS-arsenic complex may be enhanced with convective mass transport through continuous venovenous hemodiafiltration. In addition, continuous venovenous hemodiafiltration provides continuous exposure of the circulating blood volume to the dialysate and may be better tolerated by patients with hemodynamic instability. For patient 1, continuous venovenous hemodiafiltration was considered concurrent with DMPS administration, but life support measures were discontinued before its implementation. On the basis of this patient’s experience with hemodialysis, we suggest consideration of continuous venovenous hemodiafiltration for arsenic-poisoned patients given DMPS.

Plasmapheresis was also considered but was not used because the arsenic-chelator complex would be too large to be removed with this method.

CONCLUSIONS

Inorganic arsenic is a highly toxic metal that produces life-threatening conditions by inhibiting energy production and depleting energy stores. Because of the severity and rapidity with which poisoned patients develop arsenic toxicity, clinicians should administer fluid resuscitation and chelation agents presumptively, without formal laboratory confirmation. However, clinicians may be confronted by patients so severely intoxicated that they will die regardless of aggressive conventional therapies. Adjunctive approaches such as administration of DMPS, exchange transfusion, ECMO, and continuous venovenous hemodiafiltration may offer clinical benefit in situations where standard methods will fail.

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