British anti-Lewisite
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Introduction

Overview

British anti-Lewisite was developed in 1941 as an antidote to lewisite, an arsenic-based chemical warfare agent. British anti-Lewisite is used in arsenic, gold, and mercury (soluble inorganic compounds) poisoning. This drug is not indicated in patients with iron, cadmium, selenium, silver, or uranium poisoning. British anti-Lewisite is occasionally used for both acute heavy metal intoxication and Wilson disease. Parenteral British anti-Lewisite can be successfully used in lead poisoning if oral therapy fails. Experimental observations revealed that dimercaprol may be an effective neuroprotective agent.

Key points

• British anti-Lewisite is a chelating agent.
• British anti-Lewisite has a greater affinity for metal than for body proteins, and thus reverses the functioning of these proteins.
• British anti-Lewisite is used in arsenic, gold, and mercury (soluble inorganic compounds) poisoning.
• British anti-Lewisite is not indicated in iron, cadmium, selenium, silver, or uranium poisoning.
• British anti-Lewisite is administered by deep intramuscular injections of 2 to 5 mg/kg, 1 to 4 times per day for up to 10 days.
• It is no longer the preferred chelating agent.

Historical note and terminology

Lewisite (2-chlorovinylidichoroarsine) is an arsenic-based vesicant chemical warfare agent that was initially developed, although not used, by the United States during World War I. It was believed to have much greater toxicity than mustard gas, with some animal data suggesting that as little as one-third teaspoon on the skin would result in human death (Vilensky 2005). During the period between World Wars I and II, all major countries developed lewisite production facilities and, as World War II loomed, both Great Britain and the U.S. initiated research projects designed to develop an antidote to lewisite. On July 21, 1940, an Oxford University group of chemists reported the successful development of British anti-Lewisite (BAL) (Ord 2000). On first arrival in the United States in 1941, a series of studies was initiated to determine BAL’s biochemistry, pharmacology, experimental therapeutics, and clinical applications (Waters and Stock 1945). Improvements in synthesis resulted in the development of effective therapeutic ointments and solutions. BAL was produced during World War II by DuPont. Plans for the possible production of 200,000 pounds per year were developed (Waters and Stock 1945). During and after the war, nonmilitary uses for the heavy metal chelating action of BAL became apparent. Eagle and Magnuson found that 48 patients with severe or mild symptoms of arsenical encephalopathy were effectively treated with BAL (Eagle and Magnuson 1946). By 1947, 32 articles had been published or were in press on the therapeutic value of BAL (Ord 2000). BAL was the drug of choice for treatment of intoxication with arsenic, antimony, mercury, and gold. It was also considered effective in cases of intoxication with bismuth, copper, and nickel (Deichmann and Gerarde 1964).

In 1949, Porter found a 7-fold increase in copper excretion in 2 patients with Wilson disease and some decrease in neurologic signs after treatment with BAL (Porter 1949). In 1951, Cummings at the National Hospital, Queen Square, and Denny-Brown and Porter at Boston City Hospital conducted studies on the long-term effects of BAL in 4 and 5, respectively, patients with Wilson disease. The effects were definitive and dramatic; the patients exhibited great
improvement in accordance with marked increases in urinary copper excretion (Cummings 1951; Denny-Brown and Porter 1951). BAL’s use as the primary treatment for Wilson disease was short-lived because Walshe, in 1956, showed the value of the less toxic chelating agent, penicillamine (Walshe 2009). Other agents have been developed since (Brewer 1999). Nevertheless, BAL may still have some therapeutic value in patients who do not respond well to more modern agents (Scheinberg and Sternlieb 1984). It has been postulated that, because BAL is nonpolar, it may accelerate the removal of copper from within the brain compared to more modern agents (Scheimberg and Sternlieb 1984; Walshe 1999).

BAL is not generally recommended for use today because more efficient and safer chelators for oral or parenteral administration have been developed (Andersen 1999; Blanusa et al 2005; Archer 2008). In the United States it is marketed by Akorn as BAL in Oil® in 3 mL 100 mg/mL single-use ampoules (the solute is peanut oil).

**Pharmacology**

**Chemically, BAL is 2,3-dimercaptopropanol. It is a viscous, oily liquid with the offensive odor of mercaptans. It is moderately soluble in water but highly soluble in vegetable oils. BAL is a dithiol compound highly reactive with arsenic and other heavy metal compounds. It has a higher affinity for these compounds than body lipids (Merck &Co 1968; Vilensky and Redman 2003). Because BAL is unstable and susceptible to oxidation, there are storage difficulties as a ready-to-use preparation (Andersen 1999).**

BAL is administered intramuscularly. More than 50% of those receiving BAL suffer side effects, most of which are not serious and abate with discontinuation of treatment.

**Pharmacodynamics.** BAL contains 2 sulphhydryl groups that react to form a stable, generally nontoxic chelate with heavy metals, particularly arsenic, mercury, lead, and tin. The combined compound prevents the metal from reacting with sulphhydryl groups in physiological proteins and thereby renders them inert until they are excreted.

**Pharmacokinetics.** BAL is most effective when injected soon after exposure, because it more effectively prevents inhibition of sulphhydryl enzymes than reactivation of them (Blanusa et al 2005). Peak blood levels occur within 30 to 60 minutes of intramuscular injection. Highest concentration is in the liver and kidneys. Animal data suggest that 40% to 60% is excreted in urine within 6 to 24 hours. Half-life is short – excretion by 4 hours.

**Indications**

FDA-approved uses of BAL are for treatment of mild and severe arsenic toxicity, mild and severe gold toxicity, mild and severe lead poisoning (when used concomitantly with EDTA injection), and acute mercury toxicity. Chelating treatment should be started as quickly as possible, as efficacy declines rapidly as the time interval between metal poisoning and treatment increases (Kosnett 2013).

Mückter and colleagues, in 1997, published an intriguing article titled, “Are we ready to replace dimercaprol (BAL) as an arsenic antidote?” (Mückter et al 1997). The authors concluded that whereas 2 hydrophilic BAL derivatives (2,3-dimercaptopropane-1-sulphonate sodium [DMPS] and meso-2,3-dimercaptosuccinic acid [DMSA]) are less toxic than BAL and approved in several countries, in time-critical situations BAL may be more effective than these 2 compounds in restoring cellular function.

A 2004 report described the use of BAL in acute lead poisoning in a 4-year-old boy following ingestion of a lead-containing toy medallion. The child was treated with BAL and EDTA, which rapidly reduced his blood lead levels from 123 µg/dL to 57 µg/dL. He was then switched to other chelators to reduce his blood lead level still further (VanArsdale et al 2004). A report described using BAL for intentional arsenic trioxide ingestion and for intentional mercuric chloride ingestion (Wang et al 2007). In the first case, BAL (5 mg/kg) was given every 6 hours for 48 hours by deep intramuscular injection. After the first dose the patient complained of a burning sensation in the lips, throat, and mouth; lacrimation; rhinorrhea; sweating; and nausea. After a dose adjustment to 3 mg/kg every 6 hours and later to every 12 hours, there were no further adverse effects. The second patient was treated by 3 mg/kg BAL every 4 hours for 5 days. The patient developed a rash that was thought to be related to a peanut allergy and not directly to BAL. Both of these patients purchased their metal powders on the internet. It was concluded that the knowledge of aggressive decontamination, presumably using BAL, is essential. British anti-Lewisite is still being successfully used in patients with lead poisoning. Vossoughinia and colleagues treated a 19-year-old woman with severe abdominal pain, icterus, and anemia (Vossoughinia et al 2016). The patient did not respond to oral chelators, so parenteral dimercaprol and
calcium ethylenediaminetetraacetic acid (EDTA) was given. The patient responded dramatically after 5 days of treatment.

BAL is also a third-line alternative in the treatment of Wilson disease in patients intolerant to penicillamine and trientine. BAL has been reported effective in controlling unilateral rubral tremors in patients with Wilson disease refractory to 1-year therapy with penicillamine and anti-tremor medications. The tremors decreased considerably after adding dimercaprol (Chakor et al 2015).

Retained shrapnel is an uncommon cause of systemic lead toxicity. Lead foreign bodies in joint spaces may be a source of systemic lead absorption, causing elevated blood lead levels. In such patients, chelation therapy with dimercaprol can bring significant clinical improvement. Dimercaprol (British anti-Lewisite) crosses the blood-brain barrier, and chelate central nervous system lead as well (Grasso et al 2017; McAninch et al 2017; Weiss et al 2017).

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Experimental observations revealed that dimercaprol may be an effective neuroprotective agent. Acrolein is a toxic byproduct of lipid peroxidation, and it has been shown to be associated with neuropathogenesis in spinal cord injury, multiple sclerosis, and Alzheimer disease. Suppressing acrolein using acrolein scavengers has been noted as a novel strategy of neuroprotection. Dimercaprol, when administered through intraperitoneal injection, significantly reduces acrolein contents in spinal cord following a spinal cord injury in rats. Spinal cord injury in rats is a condition known to produce increased acrolein concentration (Tian and Shi 2017).

**Contraindications**

The following are contraindications for the use of BAL:

- Acute renal insufficiency that develops during therapy (use at reduced dosage with great caution or discontinue).
- Liver insufficiency, with the exception of post-arsenical jaundice.
- Iron, cadmium, or selenium poisoning (becomes more toxic when combined with agent).
- Peanut allergy (because in the U.S. it is marketed dissolved in peanut oil).

**Goals and duration of treatment**

The goal of treatment with BAL is the excretion of the poisonous metal. Treatment should be discontinued when blood levels of the metal reach safe levels, or at approximately 10 days.

**Dosing**

BAL is applied by deep intramuscular injections of 2 to 5 mg/kg, 1 to 4 times per day for up to 10 days. Specific dosages vary depending on the intoxicating metal.

**Special considerations**

**Pediatric.** BAL is recommended for use in both children and adults at similar dosing levels. Fever is a more likely side effect in children than in adults and a temporary reduction in polymorphonuclear leukocytes may also be seen in children.

**Geriatric.** There is no information available on the use of BAL in geriatric patients.

**Pregnancy.** BAL should not be used during pregnancy unless the condition is life-threatening. It is not known if BAL is present in breast milk.

**G6PD deficiency.** Patients with G6PD deficiency should not be treated with BAL unless the condition is life-threatening.

**Organic mercury poisoning.** In cases with organic mercury poisoning, BAL enhances distribution of mercury to the brain.

**Interactions**
Concurrent administration of medicinal iron should be discontinued during treatment with BAL.

**Adverse effects**

The common adverse effects of BAL are fever, sweating, headache, nausea, vomiting, increased blood pressure, tachycardia, pain and sterile abscess at the injection site, conjunctivitis, and convulsions (Rafati-Rahimzadeh et al 2014).

**References cited**


Archer SL. Dilated cardiomyopathy and left bundle branch block associated with ingestion of colloidal gold and silver is reversed by British antiLewisite and vitamin E: the potential toxicity of metals used as health supplements. Can J Cardiol 2008;24(5):397-9. PMID 18464946


McAninch SA, Adkison J, Meyers R, Benham M. Bullet fragment-induced lead arthropathy with subsequent fracture and elevated blood lead levels. Proc (Bayl Univ Med Cent) 2017;30(1):88-91. PMID 28127147


Weiss D, Lee D, Feldman R, Smith KE. Severe lead toxicity attributed to bullet fragments retained in soft tissue. BMJ Case Rep 2017;2017. PMID 28275014

**References especially recommended by the author or editor for general reading.

**Other pertinent drugs**

The following are other metal chelators (Blanusa et al 2005):
- meso-2,3-dimercaptosuccinic acid (succimer, meso-DMSA)
- 2,3-dimercaptopropane-1-sulfonic acid (unithiol, DMPS)
- D-penicillamine (DPA) and N-acetyl-D-penicillamine (NAPA)
- ethylenediaminetetraacetic acid (EDTA) and diethylenetriaminepentaacetic acid (DPTA)
- deferoxamine (DFO)
- deferiprone (L1)
- triethylenetetramine (trientine)
- N-acetyl-L-cysteine (NAC)
- iron hexacyanoferrate – Prussian blue (PB)

**Other topics to consider**

Arsenic neuropathy
Chelation therapy
Childhood lead poisoning
Lead neuropathy
Metal neurotoxicity
Occupational and environmental encephalopathies: heavy metals
Wilson disease

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