The Current Role of 2,3-Dimercaptosuccinic Acid (DMSA) in the Management of Childhood Lead Poisoning

Deborah E. Glotzer
Department of Pediatrics, Boston City Hospital/Boston University School of Medicine, Boston, Massachusetts, USA

Summary

2,3-Dimercaptosuccinic acid (DMSA) is an orally active chelating agent used in the treatment of lead and other heavy metal poisonings. In animals, DMSA chelates lead from soft tissues, including the brain, without clinically evident adverse effects or histopathological changes. In lead-poisoned children and adults, DMSA significantly increases urinary lead excretion, and, at least transiently, reduces the blood lead concentration. The safety profile of DMSA in both children and adults is encouraging, with few clinically apparent or biochemical adverse effects reported. However, clinical experience with DMSA is limited, and is not sufficient to exclude the possibility that other more serious drug-related adverse events including hypersensitivity or idiosyncratic reactions may occur. No data currently exist to determine whether drug-enhanced lead excretion with DMSA (or any other chelating agent) is beneficial in reducing lead-related neurotoxicity. The efficacy of DMSA in reducing neuropsychological morbidity, and additional safety data, are key areas requiring additional study before DMSA can be clearly recommended as the chelating agent of choice for the treatment of lead-poisoned children.
2,3-Dimercaptosuccinic acid (DMSA) is an orally-active chelating agent used in the treatment of heavy metal poisoning. The metal binding properties of DMSA have been recognised for over 30 years. The antimony chelate of DMSA was first introduced in the 1950s to treat schistosomiasis (Friedheim et al. 1954), and DMSA was identified as a potential agent for the treatment of heavy metal poisoning by researchers in the former Soviet Union (Kostygov 1958) and China (Ting et al. 1965; Wang et al. 1965). The role of DMSA in the treatment of heavy metal poisoning has been previously reviewed (Aposhian 1982, 1983; Graziano 1986). This article focuses on the role of DMSA in the treatment of childhood lead poisoning.

The suggested management of childhood lead poisoning has changed over the past 20 years (Centers for Disease Control 1991). This change was prompted by recent evidence suggesting that levels of lead exposure previously thought to represent normal and innocuous values are associated with adverse health effects including cognitive and neurobehavioural deficits (Bellinger et al. 1987; Fulton et al. 1987; Needleman & Gatsonis 1990). Prevention of childhood lead poisoning through screening programmes, counselling of families about potential lead hazards, and environmental remediation to reduce lead exposure is essential. Unfortunately, substantial numbers of children continue to be exposed to excessive levels of lead and its toxic effects. For many of these children chelation is often recommended to enhance lead excretion.

No consensus exists regarding the preferred treatment strategy for low-level lead poisoning in children. There is substantial variability in the minimum blood lead concentration for which chelation is advised and in the treatment regimens recommended to reduce an elevated lead burden (Glotzer & Bauchner 1992). There are insufficient data available to determine which chelating agent, if any, is the most appropriate treatment for a child with a given lead concentration, except in children with severe plumbism for whom treatment with calcium disodium ethylenediamine tetraacetate (edetic acid; EDTA) and 2,3-dimercapto-1-propanol (BAL) is usually recommended (Chisolm 1968; Centers for Disease Control 1991). The decision to use a particular chelating agent in the treatment of a child with an increased lead burden must be based on the blood lead concentration, the expected efficacy of the chelating agent in the range of the child's blood lead elevation, contraindications for the use of the agent in the child, and the clinician's knowledge of and experience with the agent in question. The availability of DMSA has significantly added to the armamentarium of chelating agents (BAL, EDTA and penicillamine) which can be used to promote excretion of lead more rapidly than normal excretory processes.

1. Animal Studies

1.1 Efficacy

The efficacy of DMSA has been studied in several animal models. Significant increases in urinary lead excretion following oral and intraperitoneal DMSA administration have been demonstrated in two rat models of lead poisoning (Graziano et al. 1978a; Cory-Slechta 1988). However, 20% less lead was excreted following oral DMSA compared with intraperitoneal administration (Graziano et al. 1978b). Table I summarises the results of several studies which have investigated the effects of DMSA chelation on the pattern of lead mobilisation in lead poisoned animals. All studies demonstrate reductions in the lead concentration of various tissues, although there are some inconsistencies in results among studies. While the majority of studies have administered DMSA intraperitoneally, work by Xu and Jones (1988) suggests that lead is even more effectively mobilised from bone and brain when the drug is given orally, with no significant compensatory increase in lead uptake in other soft tissues. Thus, these animal studies indicate that DMSA appears to effectively chelate lead from soft tissues including the brain even with oral administration.

The reductions in tissue lead concentration observed immediately following DMSA treatment were not observed when rats were sacrificed 4