Quelação do chumbo com DMSA – Ácido dimercaptosuccínico

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Use of oral dimercaptosuccinic acid (succimer) in adult patients with inorganic lead poisoning.

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BACKGROUND: Chelation therapy has been used as a means of reducing the body burden of lead for five decades. Intravenous sodium calcium edetate has been the preferred agent, but there is increasing evidence that dimercaptosuccinic acid (DMSA) is also a potent chelator of lead. METHODS: Oral DMSA 30 mg/kg/day was administered to adults with blood lead concentrations > or = 50 microg/dl. The impact of DMSA on urine lead excretion, on blood lead concentrations and on symptoms was observed. The incidence and severity of adverse effects was also recorded. RESULTS: Thirty-five courses were given to 17 patients. DMSA significantly ($P < 0.0001$) increased urine lead excretion and significantly ($P < 0.0001$) reduced blood lead concentrations. Mean daily urine lead excretion exceeded the pre-treatment value by a median of 12-fold with wide variation in response (IQR 8.9-14.8, 95% CI 10.1-14.6). Pre-treatment blood lead concentrations correlated well with 5-day urine lead excretion. Headache, lethargy and constipation improved or resolved in over half the patients within the first 2 days of chelation. DMSA was generally well tolerated, but one course was discontinued due to a severe mucocutaneous reaction. There was a transient increase in alanine aminotransferase (ALT) activity during 14% of chelations. DMSA caused a significant increase in urine copper ($P < 0.0001$) and zinc ($P < 0.05$) excretion. CONCLUSION: Oral DMSA 30 mg/kg/day is an effective antidote for lead poisoning, though there is a wide inter- and intra-individual variation in response.
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Dimercaptosuccinic acid (succimer; DMSA) in inorganic lead poisoning.

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INTRODUCTION: This article reviews data on the efficacy of succimer (dimercaptosuccinic acid, DMSA) in the treatment of human inorganic lead poisoning, the adverse effects associated with its use, and summarizes current understanding of the pharmacokinetic and pharmacodynamic aspects. METHODS: Medline, Toxline, and Embase were searched and 912 papers were identified and considered. PHARMACOKINETICS AND PHARMACODYNAMICS: DMSA is absorbed rapidly but incompletely after oral administration, probably through an active transporter. There is evidence that enterohepatic circulation occurs. Most DMSA in plasma is protein (mainly albumin)-bound through a disulfide bond with cysteine; only a very small amount is present as free drug, which is filtered at the glomerulus then extensively reabsorbed into proximal tubule cells. Nonfiltered protein-bound DMSA in peritubular capillaries is also available for uptake into proximal tubule cells by active anion transport at the basolateral membrane. DMSA therefore accumulates in the kidney where it is extensively metabolized in humans to mixed disulfides of cysteine. Some 10-25% of an orally administered dose of DMSA is excreted in urine, the majority within 24 h and most (>90%) as DMSA-cysteine disulfide conjugates. It is not known whether protein-bound DMSA can chelate lead; there is evidence that the mixed disulfides of cysteine are the active chelating moiety in humans. If this is the case, this suggests that chelation occurs principally, if not exclusively, in the kidney. DOSE: DMSA 30 mg/kg/day is more effective than either 10 or 20 mg/kg/day in enhancing urine lead excretion. DURATION OF THERAPY: Initial clinical studies with DMSA involved the administration of a 5-day course of treatment. Subsequently, a 19- to 26-day regimen was introduced with the intent of preventing or at least blunting a rebound in the blood lead concentration. Studies suggest, however, that repeated courses of DMSA 30 mg/kg/day for at least 5 days are equally efficacious if a treatment-free period of at least 1 week between courses is included to allow redistribution of lead from bone to soft tissues and blood. There is also evidence that in more severely poisoned patients DMSA 30 mg/kg/day can be given for more than 5 days with benefit. EFFICACY: DMSA 30 mg/kg/day significantly increases urine lead elimination and significantly reduces blood lead concentrations in lead-poisoned patients, though there is substantial individual variation in response. Over a 5-day course, mean daily urine lead excretion exceeds baseline by between 5- and 20-fold and blood lead concentrations fall to 50% or less of the pretreatment concentration, with wide variation. Maximum enhancement of urine lead elimination typically occurs with the first dose. Most symptomatic patients report improvement after 2 days of treatment. However, DMSA did not improve cognition in children < 3 years old with mild lead poisoning, presumably because lead-induced neurological damage occurred during development in utero and/or early infancy. DMSA IN PREGNANCY AND IN THE NEONATE: DMSA is not teratogenic but did produce maternal toxicity (decreased weight gain) and fetotoxicity when given in high dose (100-1,000 mg/kg/day) in experimental studies. For this reason sodium calcium edetate is generally preferred in pregnancy. ADVERSE EFFECTS: A transient modest rise in transaminase activity during chelation occurs in up to 60% of patients but has not resulted in clinically significant sequelae. Skin reactions occur in approximately 6% of treated patients and are occasionally severe. DMSA also increases urine copper and zinc excretion but not to a clinically important extent. CONCLUSIONS: DMSA is an effective lead chelator that primarily chelates renal lead. It is generally well tolerated but may occasionally cause clinically important adverse effects. DMSA may now be considered as an alternative to sodium calcium edetate, particularly when an oral antidote is preferable.
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Succimer (meso-2,3-dimercaptosuccinic acid (DMSA)) treatment of Andean children with environmental lead exposure.

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The authors studied children in Andean villages contaminated by a lead-glazing cottage industry. Mean blood lead (PbB) level in 35 exposed children, aged 3-14 years, a year before treatment, at the time of initiation of a comprehensive lead education and prevention program, was 53.4 microg/dL. PbB levels immediately before and three weeks after a ten-day regimen of succimer treatment of the 35 children were 43.4 microg/dL and 34.3 microg/dL, respectively, showing a 21% reduction and a significant difference between means ($t = 5.09$, $p = 0.0001$). PbB levels of the same children a year before treatment and immediately pre-treatment were also significantly different ($t = 10.59$, $p = 0.0001$). Thus, a ten-day course of succimer chelation effectively reduced PbB in children with moderate to severe Pb intoxication, and the education and prevention program, initiated with parents, health care providers, and educators, also contributed significantly to reducing PbB.
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Lead poisoning in children.

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Increased lead exposure and increased body burden of lead remains a significant problem for children in the United States. With the increased use of blood level screening methods, a large percentage of children in many industrialized countries are being tested as a being at risk. A controversy continues over the definition of what population to screen and at what age to screen. There are parts of the United States, especially rural areas and health maintenance organization populations, where screening for lead exposure has not been productive. A new drug, DMSA (meso 2,3-dimercaptosuccinic acid) has been approved for oral chelation of children with increased body burden of lead. At the present time it is labeled for use in children with blood lead concentrations in excess of 45 micrograms/dL. Evidence exists that DMSA is effective in lowering the blood lead concentrations in children with levels between 25 and 45 micrograms/dL. The long-term effectiveness of chelation at lower levels is at present uncertain. There remains no substitution for strict environmental decontamination in the home environment of children and the workplace environment of their parents.
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