Clinical Toxicology

An oral treatment for lead toxicity

Paul S. Thomas¹ and Charles Ashton²

¹Northwick Park Hospital, Harrow, Middlesex HA1 3UJ and ²National Poisons Unit, Guy's Hospital, London SE1, UK.

Summary: Chronic lead poisoning has traditionally been treated by parenteral agents. We present a case where a comparison of ethylene diaminetetra-acetic acid was made with 2,3-dimethyl succinic acid (DMSA) which has the advantage of oral administration associated with little toxicity and appeared to be at least as efficacious.

Introduction

For many years the treatment of heavy metal poisoning has relied upon parenteral agents which themselves have a number of toxic side effects. We report a case of plumbism which shows the benefits of using 2,3-dimethyl succinic acid (DMSA), a treatment relatively new to Western countries. In our case it was used in direct comparison to the sodium-calcium salt of ethylene diaminetetra-acetic acid, which has been the best available treatment.

Case report

A 45 year old man normally resident in Bombay, India presented with two grand mal seizures. He had previously been well apart from mild diabetes mellitus diagnosed 6 months earlier.

On examination he had a temperature of 37.8°C, he had bitten his tongue and had mildly blurred fundal disc margins. He was fully conscious, and no other abnormalities were noted at that time.

A blood film was reported as showing dense abnormalities within his red blood cells, and in view of this he was given intravenous quinine for a presumptive diagnosis of cerebral malaria. Review of this film shortly afterwards showed this to be marked basophilic stippling. His haemoglobin was 9.1 g/dl., fasting blood glucose 8.8 mmol/l, alkaline phosphatase 142 IU/l (normal 35–130), bilirubin 21 µmol/l (normal < 17), aspartate transaminase 58 IU/l (normal 35–145), gamma glutamyl trans-

ferase 112 IU/l (normal < 40). His electrolytes, urea, creatinine, clotting screening chest radiograph, computed tomographic head scan and lumbar puncture were all normal.

Re-evaluation revealed lead lines on his gingival margins and a urinary porphyrin screen was positive indicating lead toxicity. Despite careful social, occupational, and recreational history no cause for his excess lead intake could be found. As he was domiciled in India it was not possible to visit his home or workplace where he sold saris.

He was treated with intravenous sodium calcium edetate 2.8 g twice daily for 5 days with a satisfactory fall in blood lead levels and rise in urinary lead excretion but developed nausea. After a further week his blood lead levels had risen again and on this occasion he was given DMSA 660 mg three times a day for 5 days orally which was equally efficacious (Figure 1). His sole complaint associated with this treatment was some upper abdominal discomfort. His haemoglobin rose to 13.2 g/dl and his liver function tests returned to normal by the twentieth day after presentation, reflecting recovery from the lead toxicity. No further courses of treatment were required as the blood lead levels measured as an outpatient were within normal limits.

Analysis of food prepared by his family and a betel nut preparation he habitually chewed all showed no abnormal content of lead. Blood lead levels of his wife and son were normal. He returned to India and remains well.

Discussion

This patient presented with grand mal seizures and was found to have the stigmata of chronic lead poisoning, anaemia and disturbed liver function...
tests, all of which are features of chronic lead poisoning. The seizures and features associated with toxicity to the bone marrow and liver responded to treatment. DMSA is a water soluble analogue of dimercaprol (British Anti-Lewisite) both of which work by binding to the heavy metal. Dimercaprol is still recommended for many metal poisonings but has the significant disadvantages of a low therapeutic index and the need for parenteral administration. There is even some evidence in mercury poisoning that brain mercury levels may be increased by the lipophilicity of the dimercaprol-mercury complex. This redistribution of a heavy metal to the brain has also been a concern in the sodium calcium edetate treatment of lead poisoning, which does not appear to occur in DMSA treatment.

DMSA has been shown to be more effective in reducing tissue and blood levels than either sodium calcium edetate or D-penicillamine in mice pretreated with lead acetate by reducing tissue and blood levels. It was also more effective than sodium calcium edetate in a small comparative study in 11 smelter workers and in a study of children.

DMSA has few side effects which are confined to upper gastrointestinal discomfort, mild change in hepatic enzymes and increased copper excretion. It is not yet clear whether it significantly affects the excretion of zinc. In contrast, sodium calcium edetate causes headache, abdominal pain, renal impairment, anaemia and febrile reactions. D-penicillamine is also nephrotoxic, produces allergic reactions, myelotoxicity, a lupus syndrome and is contraindicated in those with penicillin sensitivity. Although there are few reports of side effects of DMSA in the literature to date, some may become apparent when the drug is used more extensively. DMSA achieves satisfactory blood levels after oral administration unlike previous treatments.

There are few reports of DMSA for lead poisoning in the Western literature but the drug has been used more extensively in the Soviet Union and in China. Few of these latter reports have been translated into English but the subject has recently been reviewed by Aposthian.

In this report it is clearly seen that an equal amount of the lead is excreted by the two drugs. The rise in blood lead level after initial cessation of therapy is explained by the mobilization of lead bound to bone which then equilibrates with the blood. The majority of the body burden is within the skeleton and repeated courses of chelation therapy are often required. Sodium calcium edetate may transiently increase lead available to target tissues by direct mobilization of the bone bound pool, whereas DMSA appears to only bind lead in the tissues. DMSA also has the advantage that it may be taken orally and so repeated treatments can be taken as an outpatient.

This case demonstrates the need for close liaison with a poison centre to find the optimum treatment available and to provide data on the effects of antidotes such as DMSA and their comparison with the previous best available treatment.

References


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