Published in final edited form as:

J Matern Fetal Neonatal Med. 2010 August ; 23(8): 932–934. doi:10.3109/14767050903317708.

A safe strategy to decrease fetal lead exposure in a woman with chronic intoxication

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Abstract

During pregnancy skeletal lead is mobilized by maternal bone turnover and can threaten fetal development. The exact strategy suggested to women of childbearing age, who were chronically exposed to lead, and, thus, have high bone lead burden, is not well established. We describe 4 years of follow-up of a 29-year-old woman with chronic lead intoxication. We (a) advised her to delay conception until 'toxicological clearance', (b) treated her with multiple courses of lead chelator, DMSA, and (c) prescribed oral calcium. Patient had low blood lead and protoporphyrin level during pregnancy until delivery. Delaying conception, lead chelation, and calcium supplementation can decrease fetal exposure.

Keywords

Lead; chelation; DMSA

Introduction

During pregnancy, maternal bone turnover is high, providing calcium for the developing fetal skeleton. As a consequence, mothers with higher lead burdens release more lead from bone [1]. Lead released to maternal blood can easily cross the placenta, consistent with the increased risk of miscarriage, stillbirth and congenital abnormalities in significantly lead-exposed women [2,3]. Increased maternal lead is also associated with reduced birth weight, small head circumference, low birth length, and cognitive impairment [4]. For that reason, blood lead levels (BLL) during pregnancy can serve as an indirect marker of fetal exposure to lead.

An expert panel has recently recommended that mothers' BLL should ideally be maintained below 5 $\mu\text{g}/\text{dl}$ from conception through pregnancy [5].

Unfortunately, environmental lead pollution and other exposure sources, remain a major public health concern. Prevention of exposure to lead, especially of young women of childbearing age must be of high priority, because, once established, chronic lead intoxication is extremely difficult, to treat. There are no clear guidelines regarding the safest strategy, to reduce lead burden before pregnancy, or to limit fetal exposure during pregnancy.

Case report

A 27-year-old woman was diagnosed with lead poisoning (blood lead, 58 $\mu\text{g}/\text{dl}$) after presenting with fatigue, anemia (hematocrit, 27%), basophilic stippling, and reporting the chronic ingestion of an ayurvedic (traditional Indian) medication. Her primary care physician suspected lead exposure based on the clinical findings and the known contamination of certain Ayurvedic preparation with heavy metals [6].

Her past medical history included type II diabetes, hypothyroidism and a miscarriage 1 year before presentation.

She had been prescribed levothyroxine for her hypothyroidism, but 18 months before presentation, she replaced it with the Ayurvedic preparation ('Gaytarin'). High concentrations of lead (1200 ppm), arsenic (790 ppm), and mercury (62 ppm) were found in Gaytarin samples analyzed by x-ray fluorescence spectroscopy.

Further laboratory evaluation found markedly increased protoporphyrins – free erythrocyte protoporphyrin IX – FEP- 795 $\mu\text{g}/\text{dl}$.

Based on the measured lead content of Gaytarin and the patient's reported dosage (3 g per day), we calculated a daily lead ingestion of 3.6 mg. This is about 800 times the acceptable daily limit for adults of 4.5 μg per day. Additionally, her cumulative lead dose was estimated at 650 mg for the 18 months of reported use.

Early in her course, we determined the patient's total lead body burden using K-shell X-ray fluorescence (K-XRF). Her patellar bone lead was extremely high, peaking at 84 $\mu\text{g}/\text{g}$ (expected upper limit for her age, 30 $\mu\text{g}/\text{g}$). Her high tibial lead was also moderately elevated, peaking at 26 $\mu\text{g}/\text{g}$ (expected upper limit for her age, 20 $\mu\text{g}/\text{g}$).

The patient and her husband expressed their will to conceive, but also their genuine concern, related to lead toxicity, and asked for the safest way to avoid fetal and neonatal exposure.

To accomplish that goal, the patient entered a strict follow-up program in an occupational clinic that specializes in lead exposure. We followed the patient for about 4 years synchronizing the occupational clinic, the bone lead laboratory, the obstetrician clinic and her primary physician.

Treatment plan had three steps:

1. Delaying conception until blood lead (and optimally bone lead) is reduced, only then giving a 'toxicological clearance'.
2. Treating the patient with serial, 19-day courses of 2,3-dimercaptosuccinic acid (DMSA) – 500 mg twice daily. The patient's initial response to DMSA chelation was excellent with resolution of her fatigue and marked improvements in blood

lead (Figure 1), protoporphyrins and hematocrit. These serial, 3 week DMSA chelation courses (500 mg twice daily) with 2–3 week rest periods were continued over most of the next 2 years. During chelation, bone lead levels were determined by k-XRF every 4–5 months on the same instrument. The effects of the prolonged therapy on bone lead burden were inconsistent with minimal net change.

3. We discontinued chelation treatment after 2 years, and the patient was started on a high dose of elemental calcium, 1200 mg/day to blunt bone turnover and any associated lead mobilization.

Only then, about 2.5 years from her first visit, she was given our advise to stop contraception and conceive. We followed her BLL and FEP during pregnancy as well. At 5th month of gestation she had BLL-9 $\mu\text{g}/\text{dl}$ and FEP-52 $\mu\text{g}/\text{dl}$. There was mild decrease at 8th month of gestation with BLL-8 $\mu\text{g}/\text{dl}$ and FEP-32 $\mu\text{g}/\text{dl}$.

On December 2008, our patient delivered a healthy (8 lbs) child, after a C-section, done because of failure to fully dilate.

Discussion

Apart from prevention of exposure, none of the chelating agents, neither calcium supplementation, has been proved to improve fetal or neonatal outcome. This single case report, obviously, doesn't prove their efficacy either.

However, as we encountered both an objective evidence of high bone and tissue lead burden, as well as deep concerns, expressed by the patient and her spouse regarding lead teratogenicity, we established a 'safe approach', that, carries minimal risks and has most chances of diminishing lead adverse consequences on pregnancy.

Reducing blood lead by repeated chelations can be done only before pregnancy, because of the potential teratogenicity of available chelating agents. Therefore, it mandates deferral of conception.

In the present case, we chose DMSA as a treatment due to its advantages of oral administration and low toxicity.

The redistribution of lead from soft tissues (intermediate pool lead) as well as exchanges between trabecular bone (represented by the patella) and cortical bone (represented by the tibia) may explain the pattern of fluctuations in bone lead that we observed in over time. A reduction in blood and soft tissue lead should be followed by a blood rebound, as lead moves from bone back to blood. In theory, during repeated chelations, the transfer of lead from bone to blood would continue until a new blood:bone equilibrium was reached at a lower concentration for both tissues [6,7].

Thus, it is likely that prolonged chelation was effective in decreasing our patient's large intermediate stores. The treatment may have been effective to the extent that the patient's final body burden of lead (in the absence of prolonged chelation) would have been much higher as soft tissue and blood lead redistributed to the bone pool.

Finally, supplementation with calcium before and during pregnancy, to decrease bone turnover, can potentially decrease lead's effects even further [8,9].

In conclusion, currently available therapies have not been shown to reliably or definitively reduce lead body burden as assessed by bone lead. At present, effective measures to minimize maternal-fetal lead transfer are limited. These include the primary prevention of

maternal lead exposure; the more rapid cessation of identified exposure sources and the early and aggressive treatment of intoxication. Despite that, when we face the challenge of high lead burden in a young woman, the triad of repeated DMSA chelation, encouraging conception only at low levels of BLL and calcium supplementation, maintaining a positive calcium balance during conception, pregnancy and breastfeeding, this strategy may reduce the risk of fetal and neonatal insult.

Acknowledgments

The authors thank Janet Paquin and her staff at the U.S. Regional Environmental Protection Agency Laboratory for analyzing the Ayurvedic Medication for heavy metals. They also thank Michael Sirois and Steve Oliveira at the Harvard Metals Epidemiology Research group facility for the K-XRF bone lead estimates. The involvement of Dr. Hu and measurement of bone lead by K-X ray fluorescence was supported by NIEHS R01-07821 and NIEHS R01-05257.

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Figure 1.
Changes in blood lead level over the course of 2 years of intermittent chelation.