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Three patients with lead poisoning following use of a Chinese herbal pill

服用一種中藥丸後導致鉛中毒的三名病人

We report on three patients with lead poisoning following use of the Chinese herbal pill Bao ning dan, prepared by the same traditional Chinese medicine practitioner. The patients had varying degrees of exposure to Bao ning dan and different clinical manifestations. Blood lead concentrations did not correlate with clinical severity. Two patients received chelating therapy and blood lead concentrations subsequently rapidly decreased. One patient was managed conservatively and end-organ complications resolved gradually. With increasing use of traditional Chinese medicines, related adverse reactions are expected to become increasingly common. Practitioners of western medicine should remain alert to this possibility. A comprehensive drug review, including the use of herbal medicines, should form a routine part of medical history taking.

本文報告了三名病人分別服用由同一中醫師配製的中藥丸"保寧丹"後導致鉛中毒的病例。這三名病人服用"保寧丹"的劑量各不相同，其臨床徵狀也不一樣。而血液鉛濃度與病情嚴重性亦不相關。兩名病人接受了螯化治療後，血液鉛濃度迅速下降。餘下一名病人接受了保守治療，其器官併發症亦逐漸回復。隨着傳統中藥使用日漸普及，與中藥相關的不良藥物反應可能會日漸常見。西醫對這種可能性應提高警覺，在向病人問取藥物史時，應經常包括中藥的使用。

Introduction

The ancient Greeks were the first to describe lead poisoning. Hippocrates reported abdominal colic in a man who extracted metals.[1] In the industrial era, paint and batteries became the main sources of lead poisoning. In Asia and Latin America, however, lead-containing folk medicines currently remain a threat to public health. Chan et al[2] reported a case of acute lead poisoning in a 4-month-old infant given Po ying tan to aid sleep. Markowitz et al[3] described an adult Korean who experienced lead poisoning after taking Hai ge fen (clamshell powder). Hai ge fen was used in this case to treat a minor gastrointestinal ailment. The clams used were probably harvested from an area polluted by heavy metals. Two further cases of lead poisoning have also been reported in Taiwan in patients who had taken contaminated 'Cordyceps', a herbal medicine.[4]

We report on three patients with lead poisoning who had taken Bao ning dan, made by one TCM practitioner in Tin Shui Wai in the New Territories of Hong Kong. One of the cases has previously been reported in a Department of Health circular.[5]

Case reports

Case 1

A 23-year-old, previously healthy woman was admitted to Tuen Mun Hospital to investigate non-specific musculoskeletal pain of 3 days' duration. Physical examination was unremarkable except for notable pallor. Haemoglobin level was 72 g/L (normal range, 120-150 g/L), with normochromic and normocytic indices. The reticulocyte count was grossly elevated to 0.12 (normal range, 0.005-0.015) proportion of red blood cells. Total white blood cell and platelet counts were normal. The lymphocyte count was low at 1.0 x 10^9/L (normal range, 1.0-4.8 x 10^9/L).

Key words:
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A peripheral blood smear showed polychromasia, anisocytosis, target cells, and basophilic stippling. Bone marrow biopsy revealed increased sideroblasts and occasional ringed sideroblasts. The serum alkaline phosphatase level was 138 U/L (normal range, 50-120 U/L) and the serum alanine aminotransferase level was 181 U/L (normal range, 10-40 U/L). The albumin level and prothrombin time were normal. Ultrasonography revealed a normal liver, and viral hepatitis markers including hepatitis A, B, and C were all negative.

Lead poisoning was suspected. The first blood lead concentration was 3.03 μmol/L (normal level, <1.21 μmol/L). A more detailed drug history was then taken. The patient admitted that she had been taking Bao ning dan, four to six pills daily for 2 months. This had been prescribed by a TCM practitioner for acne. The herbal pill was analysed by the laboratory of the Department of Health and found to contain excess lead.

Chelating therapy was not given because of altered liver function. The patient stopped taking the herbal pills and her liver function normalised within 3 weeks. The patient's haemoglobin level rose from 72 g/L to 106 g/L within 5 weeks, and was 124 g/L when measured 4 months later. Blood lead concentration remained at approximately 3 μmol/L over the first month, decreased to 2.12 μmol/L after 3 months, and was 1.66 μmol/L when measured 4 months later.

Case 2

A 35-year-old housewife, with an anxiety disorder of 8 years' duration, was receiving regular treatment from a Hospital Authority Psychiatry Clinic. She had consulted the same TCM practitioner as in case 1 and was taking Bao ning dan, believing that it would "help excrete the toxin of the psychiatric medication from her body and stop her left groin pain". She had been taking four pills daily for 6 months.

The patient had her blood lead concentration measured after she learned that Bao ning dan contained excess lead. Her first blood lead concentration was 5.6 μmol/L. She was referred to Tuen Mun Hospital by the Department of Health for further management.

On admission, she was asymptomatic apart from non-specific malaise. Physical examination was unremarkable. Her haemoglobin level was 118 g/L, with normochromic and normocytic indices. A peripheral blood smear showed no basophilic stippling. Her renal and liver function tests were normal.

She was treated initially with intramuscular dimercaprol (British antilewisite; BAL) 150 mg, but she developed facial flushing and chest tightness after the first dose. An adverse drug reaction was suspected and BAL was withheld. An intravenous infusion of calcium disodium edetate (EDTA) 50 mg/kg/d was then given for 5 days. The patient tolerated the course of treatment well. Her blood lead concentration decreased to 3.18 μmol/L and she was then discharged at her request.

Case 3

A 48-year-old housewife with symptoms of common cold had consulted the same TCM practitioner as in case 1 and case 2. She had taken four Bao ning dan pills daily for 3 days and received blood lead screening from the Department of Health after learning that the pills contained excess lead. Her blood lead concentration was 6.7 μmol/L. She was referred to Tuen Mun Hospital for further management.

She was asymptomatic apart from common cold symptoms. Her haemoglobin level was 98 g/L, with normochromic and normocytic indices. Basophilic stippling was not seen in the peripheral blood smear. She was treated with BAL and an EDTA infusion, as recommended in a standard reference (Table 1).[6] On discharge, her blood lead concentration had decreased to 1.23 μmol/L.

Discussion

The three patients had varying degrees of exposure to Bao ning dan. The first patient took the pills for 2 months and, despite her blood lead concentration being the lowest, she developed liver derangement and severe anaemia. The second patient had the longest exposure to Bao ning dan, but was asymptomatic. She had a normal haemoglobin level and normal liver function (Table 2). The third patient took Bao ning dan pills for only 3 days, but had the highest blood lead concentration. This signifies that blood lead concentration, duration of exposure to Bao ning dan, clinical symptoms, and end-organ complications may not necessarily relate to one another.

The timing of the last Bao ning dan dose may also have affected measured blood lead concentration. The highest blood lead concentration in the third patient may have

Table 1. Summary of the management of lead poisoning*

Management of lead poisoning[6]
1. Withdrawal from exposure
2. In acute oral poisoning
Activated charcoal
Gastric lavage if ingested within 1 hour
Whole bowel irrigation if radiopaque in abdominal radiograph
3. Start chelation therapy if blood lead level >450 μg/L (>2.2 μmol/L)
(a) Dimercaprol (British antilewisite)
3-5 mg/kg deep intramuscular injection
every 4 hours for 2 days
every 4 to 6 hours for 2 further days
every 4 to 12 hours up to an additional 7 days; and
(b) Calcium disodium edetate
50 mg/kg/d diluted in 500 mL 5% dextrose or normal saline intravenous infusion over 3 or more hours to a maximum of 3 g/d for 5 days
NB For encephalopaphy, first institute dimercaprol followed 4 hours later by calcium disodium edetate

* More detailed information can be found in Ellenhorn's medical toxicology. 2nd ed. Williams & Wilkins; 1997

Table 2. Clinical data summary

Patient	Duration of exposure	Lead level at diagnosis (μmol/L)	Haemoglobin level at diagnosis (g/L)	Liver impairment	Chelating therapy	Lead level on discharge (μmol/L)
1	2 months	3.03	72	Yes	No	2.94
2	6 months	5.60	118	No	Yes	3.18
3	3 days	6.70	98	No	Yes	1.23

resulted from acute lead intake. Time is required for lead to distribute to body tissues. This might explain why the third patient had no clinical features of lead poisoning, despite having the highest blood lead concentration. In long-term lead exposure, as seen in the first and second patients, the lead 'load' had distributed to the tissues and blood lead concentrations were thus more modest.

The clinical features of lead poisoning are summarised in Table 3. Specific physical signs of lead poisoning, such as gum lines and motor neuropathy were absent in this case series. Nerve conduction studies, if undertaken, may have detected subclinical motor neuropathy.

Due to impaired liver function, the first patient did not receive chelating therapy. Hepatic damage is, however, not a usual feature of lead poisoning and is not a contraindication to chelating therapy. As the patient had end-organ damage, another chelating agent such as penicillamine could have been considered. Despite the conservative approach taken, liver function recovered within 3 weeks. The patient's haemoglobin level began to improve 5 weeks later. Blood lead concentration gradually decreased to normal over 4 months in this patient. Organ recovery preceded the decrease in blood lead concentration.

The second and third patients, although relatively asymptomatic, were given chelating therapy. An EDTA mobilisation test can be used to determine whether chelating therapy is necessary.[7] This test measures the urinary excretion of lead over 8 hours after EDTA is given. The amount of lead (μg) excreted per mg of EDTA given is calculated. If the ratio is above 0.6, chelating therapy is indicated.

After absorption, lead is distributed in the circulation, mainly in the bound form. Lead binds to the porphyrin ring of haemoglobin.[8] Thus, whole blood instead of plasma lead concentration is used as the reference for toxicity. In chronic poisoning, lead is deposited first in the soft tissues, although later, most will remain in cortical bone and teeth. Because blood lead is freely exchangeable only with soft-tissue lead and part of the lead load in bone,[8] blood lead concentration does not represent the whole body lead load. This explains the apparent discordant relationship between blood lead concentrations and the degree of lead exposure seen in patients in this study. Lead deposition in cortical bone can extend the half-life of lead in the body to years.[8]

Table 3. Clinical manifestations of lead poisoning in adults[8]

Clinical severity	Blood lead level (μmol/L)
Severe Encephalopathy—coma, fit Motor neuropathy Abdominal colic Anaemia Nephropathy	>4.8
Moderate Headache, memory loss Anorexia, constipation, colic Myalgia, arthralgia	>3.84
Mild Malaise, poor concentration	>1.92

It is unclear what should be done if patients have a rebound increase in blood lead concentrations after chelating therapy. This rebound increase represents continuous mobilisation of deposited lead into the circulation. A further course of chelating therapy can be given, or alternatively, conservative management can be adopted. The authors recommend the latter approach if patients are asymptomatic and if organ damage continues to show signs of recovery.

Conclusion

Following the registration of TCM practitioners in Hong Kong, TCM is likely to become increasingly popular with the public. As many herbal medicines are homemade, as in this case series, the constituents are not standardised or regulated. An increased incidence of TCM-related adverse reactions or poisoning is foreseeable. Practitioners of western medicine should be alert to this possibility in patients presenting with non-specific symptoms. Routine medical history taking should thus include obtaining comprehensive details about herbal medicine use.

References

1. Goyer RA. 'Lead' in toxic effects of metals. In: Klassen CD, Amdur MO, Doull J, editors. Toxicology-basic science of poisons. New York: Macmillan; 1986:623-42.
2. Chan H, Billmeier GJ Jr, Evans WE, Chan H. Lead poisoning from ingestion of Chinese herbal medicine. Clin Toxicol 1977;10: 273-81.
3. Markowitz SB, Nunez CM, Klitzman S, et al. Lead poisoning due to hai ge fen. The porphyrin content of individual erythrocytes. JAMA 1994;271:932-4.
4. Wu TN, Yang KC, Wang CM, et al. Lead poisoning caused by contaminated Cordyceps, a Chinese herbal medicine: two case reports. Sci Total Environ 1996;182:193-5.
5. Department of Health. Circular 5 February, 2001. Department of Health, Hong Kong; 2001.
6. Henretig FM. Lead. In: Goldfrank LR, editor. Goldfrank's toxicologic emergencies. 6th ed. Stamford: Appleton & Lange; 1998:1319-32.
7. Markowitz ME, Rosen JF. Assessment of lead stones in children: validation of an 8-hour CaNa2EDTA provocative test. J Pediatr 1984; 104:337-41.
8. Philip AT, Gerson B. Lead poisoning—Part II. Effects and assay. Clin Lab Med 1994;14:651-70.