

Accidental ingestion of sodium molybdate at the workplace followed by short-term biomonitoring

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ABSTRACT

Introduction: Most of the molybdenum (Mo) is used in metallurgical applications, the tetrathiomolybdate form is an experimental chelating agent for Wilson's disease. Human data of acute Mo exposure are lacking and, no report of no-observed-adverse-effect level (NOAEL) has been described until now. **Case study:** We report a case of acute occupational exposure to molybdenum, with the related plasma and urine molybdenum concentrations, caused by an accidental ingestion of a sip of an anti-corrosion liquid for metal containing sodium molybdate. Our purpose was to evaluate potential systemic toxicity of molybdenum and to evaluate the dose-response/dose-effect relationship. We estimated the amount of ingested molybdenum to make a mg/kg relationship and performed repeated urine and plasma molybdenum determinations. The patient was hospitalized for three days to monitor possible development of acute symptoms/biochemical alterations. **Discussion:** We estimated the amount of the sip around 50 ml, with an estimation of a total of 5 gr of sodium molybdate that, for the patient bodyweight of 80 kg, would mean 62,5 mg/kg of ingested Mo. Blood and urine samples collected 2 hours after ingestion showed 50 mcg/L (reference range: 0.43 – 1.8 mcg/L) and 630 mcg/L (reference range: up to 116 mcg/L) of Mo respectively, confirming acute exposure. The patients remained asymptomatic confirming that an estimated oral dose of Mo of 62.5 mg/kg was not associated with adverse effects. **Conclusions:** Our value, being extrapolated by a single case, will require further confirmations from other studies to allow a full evaluation of a NOAEL. Nevertheless, it does not preclude its use in evaluating the probable absence of adverse effect in the context of acute Mo exposure.

INTRODUCTION

Molybdenum is a metal discovered in 1778 by a Swedish chemist, it doesn't exist in the pure metallic form in nature and the predominant species, naturally found, are Mo(IV) and Mo(VI) [1]. Mo is a trace element essential for mammals, since being part of a complex called molybdenum cofactor

required for catalyzing the enzymatic reactions [2]. In clinical research, molybdenum, in the form of tetrathiomolybdate, was used experimentally to treat Wilson disease [3] and, in humans, absorption of Mo through the digestive system after oral intake, has been shown to be in the range of 83-98% [4], and it is excreted mainly through the kidneys with complete elimination usually requiring several

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weeks [1]. Molybdenum is primarily used in metallurgical applications, but occupational exposure is quite rare when compared to other metals [5].

Human data on molybdenum toxicity are mainly related to chronic exposure; acute exposure reports are lacking, even more so with the evaluation of plasma and urinary Mo levels; moreover, the no-observed-adverse-effect level (NOAEL) has never been calculated for Mo.

CASE STUDY

We recently had to deal with a case of accidental ingestion of molybdenum. A 36-year-old man, worker at a company that deals with boiler maintenance, accidentally ingested during worktime a complete sip of a pure industrial product, used for metal protection, that contained sodium molybdate (Mo(VI)). The sip was ingested secondary to incautious aspiration of the product from a boiler tube in which it had been put in excess. The product was a liquid substance, with a pH of 7, used to avoid corrosive phenomena caused by water over metals (particularly copper, aluminium and steel) and to prevent encrustation and gas formation in hydraulic pipes. The safety data sheet of the product was analyzed and revealed this composition: sodium molybdate at a maximum concentration of 10% and triethanolamine at a maximum concentration of 4%. We estimated the volume of the sip around 50 ml, with an estimation of a total of 5 gr of sodium molybdate that, for the patient bodyweight of 80 kg, would mean 62,5 mg/kg of Mo. At emergency department (ED) admission he presented asymptomatic, and the baseline biochemical investigations were normal. Due to the lack of clinical data about acute molybdenum exposure, he was hospitalized to monitor the possible development of clinical manifestations and/or biochemical alterations. Blood and urine samples were collected 2 hours after ingestion to perform molybdenum determinations that resulted 50 mcg/L (reference range: 0.43 – 1.8 mcg/L[6]) and 630 mcg/L (reference range: up to 116 mcg/L[6]), respectively.

Despite the high Mo concentrations, that confirmed the acute exposure, the patient remained asymptomatic during all the hospital stay with no

signs of arthralgias, systemic inflammation (PCR < 0.01) and hypertension. Biochemistry was normal except for elevated bilirubin levels (total bilirubin 3.5 mg/dL, direct bilirubin 0.7 mg/dL, indirect bilirubin 2.2 mg/dL) on the second and third day of observation. The bilirubin level is possibly due to the fact that patient fasted for 24 hours in the event that, in the presence of a gastrointestinal clinic, a gastroscopy was necessary.

The patient was discharged on day 3 after ingestion. Nine days later, a second determination of plasma and urine Mo concentration was 2.5 mcg/L and 73 mcg/L, respectively. Considering these last Mo results, and the absence of clinical manifestations, no other molybdenum dosages were performed. At one-month follow-up, the patient was asymptomatic with normal blood tests. The patient never manifested gout-like syndrome, neither in the acute phase nor at the follow-up one month after ingestion.

DISCUSSION

Beside sodium molybdate, the ingested substance contained triethanolamine that is considered a mild irritant for humans and has been studied for the possible carcinogenic effects associated with chronic exposure, without finding any positive association (IARC group 3 carcinogen) [7]. Moreover, its irritative effect appears with a concentration of 5% [7] or more, so that the product ingested by the patient, with a maximum concentration of 4%, would lack the possible irritative effects specifically associated with triethanolamine. Finally, studies conducted on rats on triethanolamine toxicity allowed the calculation of a NOAEL of 9000-10000 mg/kg/day [8], which is higher than the estimated ingested dose of our patient (25mg/kg). For this reason, our primary focus was over the possible toxicity associated with Mo ingestion since in literature there are no sufficient data to estimate the ingested dose per kilogram that could be considered safe in acute exposure. In fact, the very few data regarding Mo toxicity are about chronic exposure. From animal studies, the reported effects in case of chronic Mo exposure vary from kidney injury, liver toxicity, anemia, and induced copper deficiency with the related symptomatology [9-11].

In humans, it has been reported that chronic exposure to molybdenum could have caused gout-like symptoms, such as arthralgias, deformity of the feet, hands and knees, in people from an Armenian region that consumed crops with elevated levels of molybdenum (10-15 mg of Mo/die) [12]. Interestingly, another case report described gout-like symptoms in an electrician chronically exposed to Mo as dust during worktime; even if the authors admitted that the association between Mo exposure and the gout could be circumstantial, they also postulate a causal relationship [5]. More recently, Peng Shi *et al.* showed a correlation between elevated Mo levels in urine and the prevalence of hypertension in workers of Mo miners as compared to office workers [13]. Another study observed a correlation between third trimester maternal elevated urine Mo concentration and psychomotor neurodevelopment of children [14] and a correlation was found between urinary Mo levels and liver problems [15].

By contrast, there are no reports of acute human exposure and it's not possible to estimate any dose-response/dose-effect relationship, NOAEL or to make an evaluation of the lethal dose in humans [10]. In reverse, the evaluated oral LD₅₀ in rats is 2733 mg/kg [16]. By doing an estimate, our patient could have ingested about 62.5 mg/kg of Mo. Nevertheless, the serum concentration of Mo after the acute event was higher compared to the reference ranges (almost 28 times greater). Therefore, in our case an estimated oral dose of Mo of 62.5 mg/kg was not associated with any adverse effect. This value, being extrapolated by a single case, will require further confirmatory results from other studies and case reports, also considering other routes of exposure and chronic exposure, in order to perform a full evaluation of a NOAEL. Nevertheless, it does not preclude its use in evaluating the probable absence of adverse effect in the context of acute Mo exposure. Our patient wasn't chronically exposed to possible sources of Mo during worktime, so that our case is only characterized by an acute and single exposure to Mo.

The only alteration found in our patient was a slightly elevated total bilirubin level. This finding is quite unspecific and, for now, it's not possible to assume a causal relation with Mo exposure, moreover

the fasting he performed for the first 24 hours of observation could have also altered bilirubin levels. The clinical and biochemical controls after one month was normal with no evidence of hepatic or kidney toxicity.

CONCLUSIONS

Despite the need of further reports to confirm our observation, we believe this case could be useful for clinicians in the rare hypothesis of facing a case of acute Mo exposure, when it's possible to make an estimation of the ingested dose. We suggest, in similar cases, a conservative approach with observation for 24/48 hours to monitor the possible development of acute symptoms and biochemical alteration and to schedule a 1-month follow-up, in absence of symptoms.

Moreover, if feasible, Mo plasma and urine concentrations should be obtained in order to evaluate the correlation between the obtained values and the development of toxicity signs/symptoms to allow further evaluation of the dose-response/dose-effect relationship.

INFORMED CONSENT STATEMENT: Written informed consent has been obtained from the patient to publish this paper.

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DECLARATION OF INTEREST: The authors declare no conflict of interest.

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