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Effects of an EDTA infusion on the urinary elimination of several elements in healthy subjects

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Ethylene diamine tetraacetate calcium disodium salt (EDTA Ca Na_2), 1 g dissolved in 250 ml of 5% w/v glucose solution, was infused intravenously over 1 h into 10 healthy subjects (eight males and two females). Urines were collected over 24 h, the day before and on the day of the EDTA Ca Na_2 infusion test. The elements Al, B, Ba, Cu, Fe, Mn, Si, Sr, Zn, Na, K, Ca, Mg, S and P were measured by inductively coupled plasma optical emission spectrometry. Pb was measured by inductively coupled plasma mass spectrometry. The EDTA Ca Na_2 infusion increased the 24 h elimination of Al from 9.8 μg to 58 μg, of Fe from 66 to 121 μg, of Mn from 2.9 to 16.5 μg, of Pb from 9.8 to 56 μg and of Zn from 623 to 8847 μg. The ratio of the increase of urinary elimination induced by EDTA Ca Na_2 was about 2 for Fe, 5 for Al, Pb and Mn, and 15 for Zn.

Keywords EDTA Ca Na_2 infusion Pb, Fe, Al, Mn, Zn urinary elimination

Introduction

Ethylene diamine tetraacetate calcium disodium salt (EDTA Ca Na_2) is a chelating agent used for the diagnosis and treatment of lead intoxication (Dwyer & Mellor, 1964; Klaassen, 1985; Levine, 1979). Although it is in widespread use its effects on the urinary elimination of elements in healthy subjects have not been studied systematically. Early investigations were carried out in patients (Perry & Perry, 1959) as were more recent studies in lead poisoned children (Chilsom, 1968). Therefore, a lack of reference values prompted us to study the effects of the EDTA Ca Na_2 infusion test on the urinary elimination of several elements in healthy subjects.

Methods

The subjects of the study were eight males and two females, all hospital medical staff, age 32.4 years ± 8.8 (mean ± s.d.), body weight 66.3 kg ± 12, height 169.7 cm ± 11.0 and body surface area 1.75 m^2 ± 0.2. They were taking a normal diet and not using any medications, except oral contraceptives in the case of one of the women. They consumed alcohol only occasionally and were non-smokers with the exception of one who smoked less than 5 cigarettes per day. Informed consent for the study was obtained from each subject.

Urines were collected in 2 l plastic bottles over 24 h, under outpatient conditions, the day before and on the day of the EDTA infusion. Before use, the bottles were carefully cleaned by rinsing with a solution of EDTA and demineralized water, free of the elements to be measured.

On the first day there was only the 24 h urine collection. On the second day, at 09.00 h, 1 g of EDTA Ca Na_2 dissolved in 250 ml of a 5% w/v glucose solution was infused intravenously over 1 h into each subject in the supine position. Just before the start of the infusion, the subjects emptied their bladders. Urine was then collected for 24 h. The total volumes of urine excreted the day before and on the day of the infusion were measured and aliquots were taken for the measurement of metals and creatinine. After infusion, the subjects were allowed normal activity. A sham infusion of the glucose solution was not given because this was not a routine clinical procedure.

The elements Al, B, Ba, Cu, Fe, Mn, Si, Sr, Zn, Na, K, Ca, Mg, S and P were measured by inductively coupled plasma optical emission spectrometry (ICP/OES) using a simultaneous spectrometer (Jobin-Yvon JY 48) (Mauras & Allain, 1985; Mauras *et al.*, 1986). Pb was measured by inductively coupled plasma mass spectrometry using a Nermag instrument because we found this method to be more sensitive and reproducible than graphite furnace atomic absorption spectrometry. Creatinine was measured automatically using a kinetic method based on the Jaffé reaction.

The results are expressed in μg and mg per day and per g of creatinine and were compared using the Wilcoxon test for paired samples.

Table 1 Urinary elimination of elements (mean ± s.d.) before and after EDTA administration in 10 healthy subjects

	Before	*After* ($\mu g\ 24\ h^{-1}$)	P	*Ratio*	*Before*	*After* ($\mu g\ g^{-1}$ *creatinine*)	P	*Ratio*
Al	9.8 ± 3.9	58.2 ± 17.9	0.01	5.9	6.2 ± 2.8	40.7 ± 17.6	0.01	6.6
B	2443.9 ± 1530.4	2039.5 ± 1344.9	NS		1471.3 ± 894.7	1337.4 ± 798.1	NS	
Ba	3.5 ± 1.5	4.2 ± 1.4	NS		2.1 ± 1.0	2.8 ± 0.5	0.05	1.3
Cu	17.6 ± 9.5	18.8 ± 10.6	NS		10.0 ± 4.5	12.1 ± 5.8	NS	
Fe	66.6 ± 28.3	121.5 ± 28.3	0.01	1.8	39.6 ± 15.1	82.1 ± 18.7	0.01	2.1
Mn	2.9 ± 1.9	16.5 ± 5.5	0.01	5.6	1.8 ± 1.1	11.6 ± 5.4	0.01	6.4
Pb	9.8 ± 3.8	56.2 ± 22.6	0.01	5.7	5.9 ± 2.1	39.2 ± 20.5	0.01	6.6
Si	15580.9 ± 7585.6	13629.9 ± 6448.5	NS		9217.6 ± 3573.8	8882.4 ± 3263.4	NS	
Sr	226.2 ± 118.0	197.5 ± 70.3	NS		142.5 ± 89.8	137.7 ± 66.1	NS	
Zn	623.0 ± 323.5	8847.4 ± 3601.9	0.01	14.2	362.3 ± 151.9	6003.9 ± 2418.6	0.01	16.6
		($mg\ 24\ h^{-1}$)				($mg\ g^{-1}$ *creatinine*)		
Na	3726.8 ± 1104.1	3953.6 ± 1001.9	NS		2244.3 ± 566.8	2685.7 ± 738.5	NS	
K	3049.5 ± 1384.3	3349.9 ± 1405.0	NS		1793.2 ± 700.1	1896.1 ± 476.5	NS	
Ca	147.1 ± 52.5	182.1 ± 59.1	NS		91.4 ± 35.8	124.8 ± 46.0	0.05	1.4
Mg	81.5 ± 43.5	65.2 ± 39.1	NS		49.5 ± 23.7	43.7 ± 23.7	NS	
S	936.5 ± 178.0	811.1 ± 205.7	NS		576.9 ± 147.0	541.0 ± 88.1	NS	
P	923.8 ± 347.6	772.4 ± 304.0	NS		546.0 ± 154.2	516.2 ± 176.3	NS	

Results

Before and after EDTA infusion urine volumes were 1.493 ± 0.716 l and 1.389 ± 0.647 l, respectively, and creatinine concentrations were 1.31 ± 0.52 g l^{-1} and 1.23 ± 0.43 g l^{-1}, respectively. No statistical differences were found.

Urinary excretion of the elements, with and without EDTA Ca Na_2 infusion, is compared in Table 1.

The basal urinary elimination of the elements tested ranged from a few μg to a few g per 24 h. On average, Mn and Ba elimination was about 3 μg, Al and Pb about 10 μg, Cu 17 μg, Fe 66 μg, B 2.4 mg, Si 15 mg, and Na and K more than 3 g.

The EDTA Ca Na_2 infusion increased the 24 h elimination of Al from 9.8 to 58 μg, of Fe from 66 to 121 μg, of Mn from 2.9 to 16.5 μg, of Pb from 9.8 to 56 μg and of Zn from 623 to 8847 μg. The excretion of the other elements B, Ba, Cu, Si, Sr, Na, K, Ca, Mg, S and P was not altered. However, when the results were expressed per g creatinine, there was a slight but significant increase in the elimination of Ba and Ca. The ratio of the increase of urinary elimination induced by EDTA Ca Na_2 was about 2 for Fe, 5 for Al, Mn and Pb and 15 for Zn.

Discussion

More data are available on normal concentrations of elements in blood plasma than in urine. The 24 h excretion of Al that we observed is in agreement with literature values (Allain *et al.*, 1990). The 24 h urinary excretion of Pb (9.8 μg 24 h^{-1}) was similar to the value of Behringer *et al.* (1986) (10 μg 24 h^{-1}). The high mean concentration of 120 μg l^{-1} obtained in normal Americans (Perry & Perry, 1959) can be explained by the insufficient sensitivity of the spectrographic method used at that time. Our results for Ba, Cu, Sr, Zn are similar to recent findings (Schramel *et al.*, 1985). The 24 h excretion of Na, K, Ca, Mg is well documented and our values are in the same range as those reported, for example, by Staessen *et al.* (1983).

The increased urinary elimination of Pb, Mn and Zn after EDTA Ca Na_2 infusion is well-documented (Perry & Perry, 1959). In addition, we have now shown that the elimination of Fe and Al is also increased.

The large increase in Zn excretion (× 15) could lead to Zn deficiency and Zn supplements should be considered in patients treated by successive infusions of EDTA Ca Na_2.

The EDTA Ca Na_2 test can aid evaluation of the degree of intoxication by Pb and perhaps by Mn, Fe and Al but in patients with renal dysfunction the interpretation of results is more difficult.

In conclusion, like the desferrioxamine test that we studied recently (Allain *et al.*, 1987), the EDTA Ca Na_2 test can be useful in the diagnosis and treatment of intoxication by some elements. The present data from healthy subjects forms a basis for the quantitative evaluation of the results of the EDTA Ca Na_2 test.

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