Cadmium, lead and mercury levels in cerebrospinal fluid and risk of amyotrophic lateral sclerosis – A case-control study

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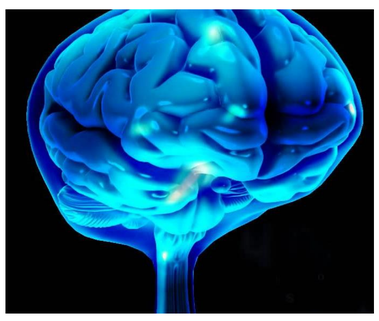
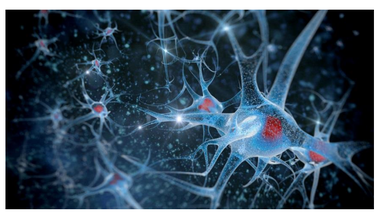
Background and aims

Many studies raised the possibility of neurotoxic effects of heavy metals and an increased risk amyotrophic lateral sclerosis (ALS) among exposed subjects. The aim of the study was to assess the levels of cadmium (Cd), lead (Pb) and mercury (Hg) in 38 newly-diagnosed ALS patients and 38 sex and age matched neurologic hospital-referred controls by using cerebrospinal fluid (CSF) as a CNS biomarker of exposure.





Methods

The 38 ALS cases included 16 men and 22 women, with mean age of 55.5 years (range 30.7–76.4 years) who underwent lumbar puncture. The 38 controls were patients who also underwent lumbar puncture, for suspected but later unconfirmed neurological disease. CSF total heavy metal content was determined using inductively coupled plasma sector field mass spectrometry (ICP-SF-MS) according to methodologies previously established for biological matrices and specifically for CSF.

Results

Median and percentile 25th - 75th percentile values for cadmium (Cd), lead (Pb) and mercury (Hg) were 71.55 ng/l (22.0 - 105.0), 132 ng/l (69.5 - 497.0) and 216.5 ng/l (32.0 - 634.0) in controls and 35.9 ng/l (24.6 - 66.8), 155.0 ng/l (70.1 - 351.0) and 195.5 ng/l (125.0 - 264.0) in ALS patients, respectively (Figure 1 and Table 1). In logistic regression analysis, we did not evidence an association between ALS risk and CSF Cd content. An imprecisely increased risk was found in crude and age-adjusted models, with ORs between the highest vs. the lowest tertiles of 1.37 (0.50 - 3.82) and 2.84 (0.75 - 10.80) for Pb, and of 4.06 (0.44 - 37.28), and 6.14 (0.57 - 65.95) for Hg (Table 2). Gender-stratified analysis shown higher risk for females than for males.

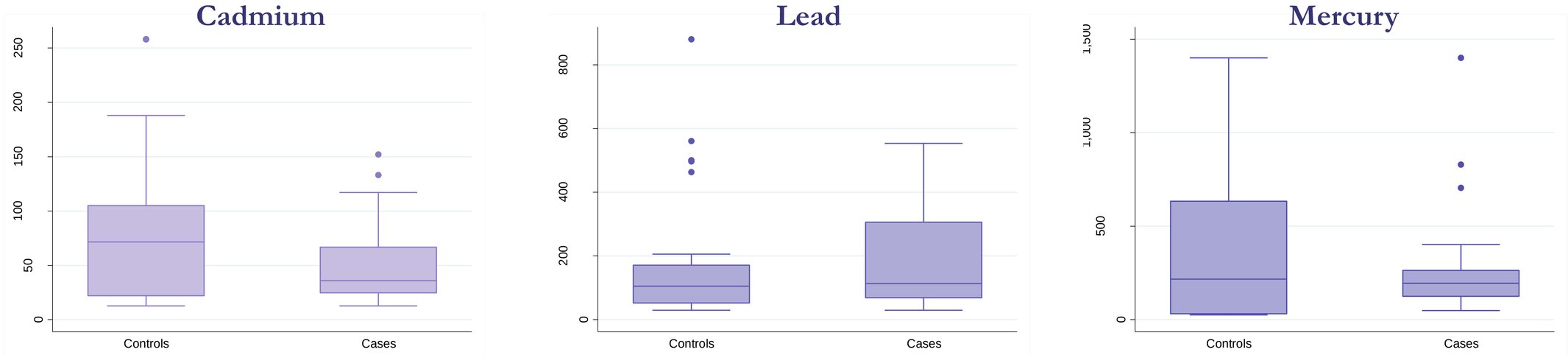


Figure 1. Box plots of heavy metals levels for cases and controls.

Metal	Percentiles 5th	25th	50th	75th	95th
Cadmium					
Controls	12.6	22.0	71.55	105.0	806.0
Cases	9.74	24.6	35.9	66.8	133.0
Lead					
Controls	27.3	69.5	132	497	7750.0
Cases	29.9	70.1	155.0	351.0	2670.0
Mercury					
Controls	21.7	32.0	216.5	634.0	1510.0
Cases	51.4	125.0	195.5	264.0	830.0

Table 1. Distribution of heavy metals in the CSF of cases and controls. All values are in ng/L.

	Crude OR	95% CI	*P trend*[b]	Adjusted[a] OR	95% CI	*P trend*[b]	Cases/ Controls
Cadmium							
≤30.99	Ref.			Ref.			16/12
30.99-82.54	1.03	(0.36-2.96)		1.14	(0.38-3.40)		16/13
>82.54	0.37	(0.11-1.24)	*0.051*	0.41	(0.12-1.43)	*0.073*	6/13
Lead							
≤86.66	Ref.			Ref.			11/12
86.66-195.72	0.83	(0.28-2.49)		1.03	(0.30-3.50)		10/13
>195.72	1.37	(0.50-3.82)	*0.485*	2.84	(0.75-10.80)	*0.556*	17/13
Mercury							
≤79.33	Ref.			Ref.			3/12
79.33-328.72	13.88	(1.65-116.74)		16.93	(1.80-159.70)		29/13
>328.72	4.06	(0.44-37.28)	*0.743*	6.14	(0.57-65.95)	*0.797*	6/13

[a]Adjusted for age
[b]*P trend* based on 1 ng/L increase

Table. Odds ratio (OR) for increasing tertiles of Cd, Pb and Hg. Tertiles cutpoint are in ng/L. Crude conditional logistic regression analysis and adjusted for age are presented.

Conclusions

Our results do not suggest a major role of exposure to cadmium in increasing ALS risk, while results for lead and mercury appear to need further investigations.

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