Bull. Environ. Contam. Toxicol. (1985) 34:170–174

Bulletin of Environmental Contamination and Toxicology

Tellurium Burden and Neurochemical Effects in Moderate Peroral Exposure

Sinikka Valkonen and H. Savolainen*

Department of Industrial Hygiene and Toxicology, Institute of Occupational Health, SF-00290 Helsinki 29, Finland

Tellurium has varied industrial uses extending from Cu-alloys for nozzles of oxyhydrogen torches and rubber compounding for improvement of its oil and temperature resistance to microchip industry in electronics. Thus, tellurium exposure may constitute a modern occupational hazard. The classical indication of tellurium exposure is the garlicky odor of breath preventable by vitamin C administration (Hunter 1974). This may be attributed to the antioxidant effect of the vitamin. High peroral tellurium doses are known to cause intense lipofuscinosis in brain (Duckett and White 1974) possibly owing to the peroxidative effect of the metalloid. Demyelination is a hallmark of the tellurium toxicity in the peripheral nervous system (Said et al. 1981; Wiley-Livingston and Ellisman 1982). Tellurium has a long half-life in the nervous system (Duckett 1982) which may allow its accumulation in continued exposure. The current literature relates to rather high tellurium doses with dramatic toxicity while it is not known whether low-level repeated dosing causes its accumulation in the critical organ and whether its absorption can be monitored quantitatively e.g. by blood analyses. To clarify this, we exposed rats to moderate level of tellurium in drinking water and developed a method for its quantitation in the biological material and followed the proposed peroxidation-related effects in brain.

MATERIALS AND METHODS

Fifteen male 3-month-old Wistar rats (380±41 g, ±S.D.) were given drinking water which contained 100 mg $TeCl_4$ per liter (371 μM) for 7 to 35 days. 15 control rats (373±35 g, ±S.D.) were given tap water. The consumption

* Correspondence and reprint requests

of liquid was measured daily. Rats were killed in groups of 5 animals after 7, 21 or 35 days by decapitation and bled in heparinized tubes. Te concentrations were analyzed as follows. Blood (1 ml) and lyophilized tissue samples (67.5-409 mg dry weight) were digested in 1 ml of sulfuric acid-perchloric acid-nitric acid mixture (1:1:3, per vol.). 20 µl tributyl phosphate served as an antifoam agent. A complete digestion was achived in 175 min while the temperature rised from 125°C to 275°C. The clear digests were washed into the hydride reaction vessel (Perkin-Elmer Hydride MHS-1) with 10 ml of 7.5 % nitric acid and 7.5 % hydrochloric acid mixture. The dihydrogen telluride was generated by adding 2.5 ml 5 % $NaBH_4$ in 2 % NaOH. Telluride was purged by argon into the heated (1000°C) quartz tube of Perkin-Elmer 400 atomic absorption spectrophotometer equipped with a Te hollow cathode lamp operated at 214.3 nm. Peak heights were used for quantitation, and the concentrations were given per g wet weight. Commercial Te standards were used (Aldrich Chemical Co., U.S.A.) The standards and blanks were treated indentically with the samples. The coefficient of variation was 14.4 % at 20.8 nmol/g dry weight (N=20) with a detection limit of 20 ng (0.07 nmol/ml). Complete recovery of added Te in samples was obtained at concentration range of 50-400 ng. The left cerebral hemispheres were also analyzed for glutathione content (Hissin and Hilf 1976), succinate dehydrogenase (Lim and Hsu 1971) and creatine kinase activities (Szasz and Gruber 1978). Statistical evaluation was made with Student's t-test.

RESULTS AND DISCUSSION

Control animals showed a very low Te burden while it accumulated promptly in the exposed rats. Blood had the highest Te concentrations with an increasing trend according to the exposure period (Table 1). Liver showed

Table 1. Tellurium burden in peroral exposure

Time (d)	Ingested dose (µmol/kg body wt)	Blood (nmol/g)	Liver (nmol/g)	Kidney (nmol/g)	Brain (nmol/g)
7	339 ± 31	30±3.5	5.7±1.3	1.4±0.3	0.7±0.2
21	600 ± 47	38±3.4	5.5±1.0	1.7±0.3	2.4±0.3
35	1025 ±115	45±5.8	5.7±0.8	2.7±0.3	3.1±0.8
Control	0	0.3±0.2	0.2±0.1	0.3±0.2	0.4±0.3

Each figure is the mean of 5 rats ± S.D. except N = 15 for controls.

similarly a rapid increase in its Te content while the kidneys and brain clearly had a continuous accumulation throughout the experiment. The brain Te (y, nmol/g) was linearly correlated to the time (x, d): $y = 0.08 x + 0.35$ ($r = 0.98$).

Brain glutathione content was above the control range at 35 days and the succinate dehydrogenase activity after 21 days (Table 2). Thus, appreciable neurochemical effect was only seen after the brain Te exceeded 2 nmol/g while no effect was found at 7 days when the brain Te did not statistically differ from the control samples (Table 1).

Tellurium shows a virtual blood-tissue barrier although it is not known whether this is caused by its affinity to blood constituents as in the case of arsenic (Valkonen et al. 1983) or whether it is truly excluded from the cells of the studied organs. Anyway, the hepatic disposal mechanism for Te is in a virtual steady state from 7 days onwards as shown by the unchanged Te content. It is probable that Te is excreted by kidneys although this might be saturable by higher doses in view of Te accumulation. The initially low uptake of Te in brain may show a true blood-brain barrier. Once incorporated in the nervous system Te has a long half-life causing the accumulation.

Neuronal mitochondria take up Te which seems to cause a process destroying them and giving rise to lipofuscin (Duckett and White 1974). Succinate dehydrogenase is a mitochondrial enzyme in the inner membrane and coupled to the respiratory chain. The increase in its activity at brain Te above 2 nmol/g might reflect these effects. However, the number of mitochondria may not have increased as the other mitochondrial enzyme, creatine kinase activity remained unchanged or tended to decrease. This discrepancy may be caused e.g. by mitochondrial swelling (Font et al. 1981).

Glutathione is one of the factors that protects the neural cells and their organelles towards the effects of lipid peroxidation (Savolainen 1979). Increase in the glutathione content may thus show attempts to counteract peroxidative effects associated with the postulated mitochondrial damage.

Our work might be used as a basis for the development of a biological exposure test for tellurium with clues as to the dose-dependent toxicity. Such a test could also be used as a chemical method to detect nuclear contamination. Tellurium was found in the European continent after the Windscale accident (Stewart and Crooks 1958).

Table 2. Neurochemical effects of tellurium intake

Time (d)	Glutathione (μmol/g)		Succinate dehydrogenase (nmol/min x mg protein)		Creatine kinase (nmol/min x mg protein)	
	Control	Exposed	Control	Exposed	Control	Exposed
7	2.1±0.24	2.0±0.12	1.9±0.11	1.9±0.19	1.5±0.13	1.6±0.15
21	2.0±0.08	2.1±0.16	1.7±0.19	2.3±0.17**	1.4±0.08	1.3±0.04
35	2.1±0.23	2.4±0.21*	1.8±0.11	2.0±0.11*	1.3±0.11	1.1±0.24

Each figure is the mean of five determinations ± S.D. *Differs from control at $P<0.05$ and **differs from control at $P<0.01$.

REFERENCES

Duckett S (1982) The distribution of ^{127m}tellurium in normal and pathological tissues of young and adult rats. Neurotoxicolofy 3: 63-74

Duckett S, White R (1974) Cerebral lipofuscinosis induced with tellurium: Electron dispersive x-ray spectrophotometry analysis. Brain Res 73: 205-214

Font B, Vial C, Goldsmith D, Eichenberger D, Gautheron DC (1981) Heart mitochondrial creatine kinase solubilization. Effect of mitochondrial swelling and SH group reagents. Arch Biochem Biophys 212: 195-203

Hissin Pj, Hilf RA (1976) A fluorometric method for the determination of oxidized and reduced glutathione in tissues. Analyt Biochem 74: 214-217

Hunter D (1974) The diseases of occupations. The English Universities Press, London, pp 457-459

Lim R, Hsu L-W (1971) Studies on brain specific membrane proteins. Biochim Biophys Acta 249: 569-582

Said G, Duckett S, Sauron B (1981) Proliferation of Schwann cells in tellurium-induced demyelination in young rats. Acta Neuropath (Berl) 53: 173-179

Savolainen H (1979) Labilization of cerebral lysosomes by autologous microsomes and protection by cytosolic fraction and a superoxide scavenger in vitro. Biochem Biophys Res Commun 86: 1222-1226

Stewart NG, Crooks RN (1958) Long-range travel of the radioactive cloud from the accident at Windscale. Nature (Lond) 182: 627-628

Szasz G, Gruber W (1978) Creatine kinase in serum: 4. Differences in substrate affinity among the isoenzymes. Clin Chem 24: 245-249

Valkonen S, Savolainen H, Järvisalo J (1983) Arsenic distribution and neurochemical effects in peroral sodium arsenite exposure of rats. Bull Environ Contam Toxicol 30: 303-308

Wiley-Livingston CA, Ellisman MH (1982) Return of axonal and glial membrane specializations during remyelination after tellurium-induced demyelination. J Neurocytol 11: 65-80

Received February 29, 1984; accepted April 27, 1984