SHORT REPORTS

Urinary excretion of platinum from platinum industry workers

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Abstract

Objectives—Assessment of level of exposure to platinum and platinum concentration in urine from platinum industry workers to evaluate internal exposures and excretion kinetics.

Methods—Platinum concentrations in urine samples from 34 workers were measured by adsorptive voltammetry after UV-photolysis. Morning and evening samples were taken two to six times during six months. Individual exposures were assessed by personal air sampling. Also, two male volunteers were exposed to platinum dust for four hours at a typical platinum refinery workplace.

Results—Urinary platinum excretion after a shift in platinum industry workers was found to be up to 6270 ng/g creatinine—that is, 1000 times above the median value of unexposed people. Urinary excretion reached the maximum nearly 10 hours after inhalative exposure to dust containing platinum. Elimination corresponded to a first half life of about 50 (95% confidence interval (95% CI) 36 to 66) hours, but there were indications that a part of the incorporated platinum is stored longer. The amount of urinary platinum excretion showed a close correlation with the exposure level monitored by personal air sampling.

Conclusions—A newly developed analytical method enabled the detection of even natural background concentrations of platinum. Thus, increased urinary platinum concentrations could be detected early, which is important to avoid damaging health of exposed workers.

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Health problems due to exposure to platinum or related salts were reported first by Karasek and Karasek¹ in 1911 and Carozzi² in 1934. Since 1945 airborne platinum concentrations at platinum refineries have been measured³ and associated with health problems,⁴ especially the risk of allergic airways reaction. In western

Germany 68 people with occupational disease from platinum salts have been registered since 1990. There are threshold limit values (TLVs) for platinum in some countries. In Germany there are two thresholds, 1 mg/m³ for metallic platinum and 2 µg/m³ for platinum salts. Nowadays, biomonitoring of metals in human tissues (blood, plasma, urine) is recommended to evaluate individual exposure of workers. In the past few years analytical techniques have been improved to the extent that it is possible to determine urinary excretion of platinum even in unexposed people.

The aim of this investigation was to evaluate urinary platinum concentrations in workers exposed to platinum salt dusts.

Methods

SUBJECTS AND SAMPLING OF URINE

Thirty four workers (32 men, two women) aged from 23 to 67 (mean 42.0) years from a platinum refinery and catalyst production company were included. Fifteen employees had a current exposure to platinum salts (mainly K₂PtCl₆ and Pt(NO₃)₂ <2 µg/m³). Four employees had stopped exposure two to six years ago (table) because of hypersensitisation to platinum. Three people were only occasionally exposed to lower levels. As a control group 12 workers of the same company without any exposure to platinum were monitored.

Sampling always included two spot urine samples, one at the end of a shift and a second one the next morning at home. Participants were instructed to follow careful washing procedures and possible contamination risks should be detected by comparison of results from sampling at the factory and at home. Within a six month period workers were investigated between one and three times.

Two male volunteers (30 and 42 years old) with normal urinary platinum excretion were exposed to platinum salt dusts for four hours by handling dry (NH₄)₂PtCl₆ powder. All urine samples from the next four days were collected separately. Later on, morning samples were taken once a week for a six month period.

All participants were informed about the proposed measurements and gave their written consent.

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Urinary excretion of platinum from two volunteers after four hours of exposure to platinum salt dusts.

AIR SAMPLING

The air sampling strategy was designed to get information about platinum concentrations of specific manufacturing procedures and not to control threshold limits. For stationary sampling (according to German guideline VDI 2463) we adjusted the fluxes to 25 l/min and for personal samplers (BIA samplers St Augustin) to 2 l/min both equipped with polycarbonate filters 0.8 μm (Millipore). Sampling lasted 0.1–3 hours with air volumes 100–5000 l.

PLATINUM MEASUREMENT

All samples were measured by adsorptive voltammetry after ultraviolet photolysis of the urine samples⁵ and microwave digestion of the filters.⁶ Limits of measurement were 2 ng/l for urine and 2 $\mu\text{g}/\text{m}^3$ for air samples, precision was better than 10%. To achieve reliable data at this fmol level internal and external quality control procedures were strictly followed.

Statistical calculations (*t* test) were performed by SPSS for Windows. Excretion kinetics evaluated by RSTRIP 4.1 (Micro-Math, USA).

Maximum (after shift) and minimum (next morning) urinary platinum excretion from workers (1) currently high, (2) formerly high, (3) currently low, and (4) not exposed to platinum dusts

Exposure group	Subject No	Urine samples	Platinum (ng/g creatinine)		Smoker	Exposure (y)
			Max	Min		
1	1	4	5370	2520	No	4
	2	4	6250	2500	No	5
	3	4	6270	1620	No	> 9
	4	4	4170	2470	No	> 9
	5	2	4020	2620	Yes	> 9
	6	6	3320	1520	No	1
	7	2	2920	1510	No	6
	8	2	2120	1750	No	5
	9	6	620	250	No	1
	10	4	1520	960	No	6
	11	2	1440	850	Yes	2
	12	2	500	480	Yes	1
	13	4	720	340	No	1
	14	2	430	270	No	5
	15	2	330	170	No	1
2	16	4	170	110	No	3 (2)*
	17	2	160	120	Yes	4 (4)*
	18	2	130	90	Yes	5 (6)*
	19	2	160	10	No	9 (4)*
3	20	4	230	40	No	> 9
	21	2	140	60	No	> 9
	22	2	18	16	No	> 9
4	23	2	12	10	No	—
	24	2	6	5	Yes	—
	25	2	4	3	No	—
	26	2	5	3	No	—
	27	2	4	3	Yes	—
	28	2	4	3	Yes	—
	29	2	4	2	No	—
	30	2	4	2	No	—
	31	2	3	2	No	—
	32	2	2	2	No	—
	33	2	2	2	No	—
	34	2	1	1	Yes	—

* (n)=Years since exposure finished.

Results

The table shows the maximum and minimum values of urinary excretion of platinum from all participants. We stratified the study group as follows: (1) current high exposure, (2) former high exposure, (3) current low exposure, and (4) control group. To consider different excretion rates from spot urine samples the platinum values were expressed in ng/g creatinine. We found that urinary excretion of platinum from workers was about 1000 times higher than control subjects (table). Air concentrations at the working places ranged from 0.2 to 3.4 $\mu\text{g}/\text{m}^3$ (stationary) and from 0.8 to 7.5 $\mu\text{g}/\text{m}^3$ (personal sampling) with mean values of 1.1 and 2.5 $\mu\text{g}/\text{m}^3$. For the control group air concentrations were <0.007 $\mu\text{g}/\text{m}^3$. Ambient air concentrations are far below this level. For example, monitoring in Munich city during the past four years showed airborne platinum concentrations around 0.00001 $\mu\text{g}/\text{m}^3$.⁶

Those employees (group 2), who had not been exposed to platinum for several years and were free from symptoms still excreted 25-fold more platinum than the control group. There may be a long term platinum pool comparable with that found in patients after cisplatin treatment.^{7,8} As expected the platinum excretion from people who had only a little contact with platinum salts (group 3) was closer to the control group. Statistically the differences

between the controls (group 4) and groups 1 and 2 or 3 are significant (t test: $p < 0.001$).

The two volunteers were exposed mainly to platinum salts ($(\text{NH}_4)_2\text{PtCl}_6$) for a four hour period, performing filtration and hand crushing procedures. Volunteer A had a more intensive contact than B, which is reflected by results of personal air sampling. The filter of person A contained 800 ng platinum compared with 60 ng for person B. Calculation of the mean air concentrations resulted in $1.7 \mu\text{g}/\text{m}^3$ for A and $0.15 \mu\text{g}/\text{m}^3$ for B. The urinary platinum excretion increased steeply (15 to 100-fold compared with initial values, figure) in the first urine samples after exposure. Platinum excretion followed an exponential decay ($t_{1/2} = 50$ h; 95% confidence interval (95% CI) 36 to 66 hours) in both participants. From person A a second half life of 24 days (95% CI 18 to 33 days) can be calculated from urinary platinum excretions from 200 to 4000 hours after exposure. At this time he excreted 12 ng/g creatinine, still above the concentrations before the exposure, but within normal values from unexposed people.⁹⁻¹⁰

Discussion

There are not many papers with values for background platinum excretion because the analytical methods of measurement of low concentrations of urinary platinum are new. Most investigations⁵⁻¹¹ agree with a range of 1–20 ng/l and median values around 5 ng/l for the unexposed population. The only study on measurement of platinum concentrations in urine from workers exposed to platinum is from 1991. Weber *et al.*¹¹ investigated 18 employees from a catalyst production company. They measured air platinum concentrations at $1.7\text{--}6.0 \mu\text{g}/\text{m}^3$ and urinary excretions at 10–2900 ng/l (median 320 ng/l). These data correspond well with our findings. From four people they analysed urine after two weeks of holiday but found no decrease in the values. They suggested that there might be slow excre-

tion kinetics, a hypothesis which is strongly supported by our data. Recently we reported that patients show increased platinum excretion eight years after the last cisplatin treatment, which is 200-fold more than the median from unexposed people.^{7,8} Although these patients received platinum intravenously instead of by inhalation the final storage of some platinum in the body could be similar. Venables *et al.*¹² found evidence that smokers have an increased risk of respiratory allergy after exposure to platinum. Our data suggest that there may be a healthy worker effect in our study group, because there was only one smoker among the eight most highly exposed people.

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