Letter to the Editor

Occupational Exposure to Indium of Indium Smelter Workers*

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Case reports of indium-related lung disease in workers have raised public concern to the human toxicity of indium (In) and its compounds. However, studies evaluating the exposure or health of workers in In smelting plants are rare. Therefore, in this study, we focused on four In smelting plants, with the main objective of characterizing In in smelter plants in China and discussing the potential exposure biomarkers of In exposure. We recruited 494 subjectsat four In smelting plants in China. Personal air samples, first morning urine and spot blood samples were collected. In concentrations in samples were analyzed using inductively coupled plasma mass spectrometry. In concentrations in air samples did not exceed the permissible concentration-time weighed average, but the smelter workers had a higher internal exposure to In. Positive correlations were observed between the air In and urine In concentrations, and between the air In and blood In concentrations. This study provides basic data for the following In exposure and health risk assessment.

Indium (In) (CAS 7440-74-6) is a rare metal that is primarily used in the form of indium-tin oxide (ITO), a sintered material consisting of 90% indium oxide (In_2O_3) and 10% tin oxide (SnO_2), to produce flat panel displays. Case reports of In-related lung disease in workers that have emerged during the past decade from Japan, China, and America have raised public concern to the human toxicity of In and its compounds[1-2]. China has achieved the highest In output since 2000, accounting for over 50% of the total global refined In[3]. In this study, we focused on four In smelting plants, with the main objective of characterizing In in smelter plants in China and discussing the potential exposure biomarkers for In smelter workers.

We selected four smelting plants of different sizes and degrees of automation in different areas. Plant 4 (P4) is a small/medium-sized plant (annual production<20 tons), plant1 (P1), plant2 (P2), and plant3 (P3) are medium/large-sized plants. Workers in P2 didn't have a fixed type of work because of the job rotation system. We identified the six main work tasks performed on the days of sampling: 1) lixiviate, 2) extraction, 3) metathesis, 4) electrolysis, 5) ingot casting, and 6) chemical examination workers. We assessed exposure using a cross sectional survey. We used questionnaires to obtain information about work tasks and the use of protective equipment on the day of sampling as well as information about lifestyle, including tobacco use and dietary habits. Personal breathing zone air samples were collected from workers over the entire shift period, with continuous sampling for three days. The blood samples were collected by registered nurses at the work places. Serum was collected in a 4 mL serum separation hose (Vacutainer SST^{TM}, BD, USA). The tubes were centrifuged at 3000 rpm for 20 min to obtain serum. The first morning urine samples (>50 mL) were collected from the participants on arrival at workplace. We stored all samples in a portable fridge at 4-6 °C until arrival at the laboratory (within 24 h), where the samples were immediately frozen at -20 °C. This study was approved by the institutional review board at the National Institute of Occupational Health and Poison Control, China CDC, and each subject gave written informed consent. All volunteers agreed to the use of their blood and urine samples for this biological monitoring survey.

Blood, serum and urine samples were analyzed by inductively coupled plasma mass spectrometry[4]. For air samples, the filters were digested in the hot

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block and analyzed by inductively coupled plasma mass spectrometry.

For statistical analyses, SPSS software version 20.0 for Windows was used. For observations below LOD, the value was imputed as LOD divided by the square root of 2[5]. The metal concentrations in the air samples were highly skewed, and therefore, we log (ln) transformed them and used parametric statistics to evaluate the results. We analyzed different work tasks with no stratification by plants, and used binary logistic regression analysis to exclude the effects of confounding factors for different plants. We used a simple one-way analysis of variance (ANOVA) and post-hoc test for multiple analyses to evaluate differences in air samples. We used non-parametric statistics on non-transformed data for the biomonitored results. The differences between two independent groups were assessed using the Mann-Whitney U-test, whereas the differences among multiple independent groups were assessed using the kruskal-Wallis H Test. The correlation analysis between concentrations in air samples and biological samples was estimated by computing Spearman's correlation coefficient. Statistical significance was established at $P>0.05$. Analytical results of urine samples with a specific gravity of <1.010 g/mL or >1.030 g/mL were excluded from statistical analysis.

In total, we recruited 494 subjects (417 smelter workers and 77 office workers) from the four In smelting plants. One Hundred and forty-six of the study participants (38.7%) were women. The age of participants ranged from 21 to 60 years (mean=39.67 years), and the work age of the participants ranged from 1 to 42 years. Among the participants, approximately 49.2% were smokers. Plants 1-3 used process ventilation, whereas P4 did not, as their building is an open workshop. All workers wore personal protective equipment during their shifts according to their company policy demands, workers in P4 wore the ordinary cotton mask, and workers in other three plants wore professional dusk mask.

We collected 190 personal breathing zone air samples from In smelting workers and 29 personal breathing zone air samples or static samples from office workers. The average sampling time was 295 min (range 120-480 min) for the samples. As shown in Table 1, the geometric mean (GM) concentrations of In in the air samples from the smelter workers in the four plants were 2.76, 0.41, 0.45, and 2.26 μg/m³, respectively. No significant difference of In concentration in smelter workers was found between P1 and P4, and between P2 and P3; the concentrations were significantly higher in P1 and P4 than those in P2 and P3 ($P<0.05$). In concentrations

Table 1. In Concentrations (μg/m^3) in the Collected MCE Fraction from Personal Air Sampling of Workers

Group	N	GM	GSD	MIN	MAX	*P*
P1						
Office workers	8	0.45	4.85	0.12	18.85	0.010
Smelter workers	90	2.76	4.56	0.09	69.05	
P2						
Office workers	2	0.23	1.56	0.17	0.31	0.507
Smelter workers	54	0.41	3.40	0.02	2.81	
P3						
Office workers	3	0.13	4.84	0.05	0.80	0.061
Smelter workers	31	0.45	2.71	0.03	6.71	
P4						
Office workers	2	0.82	2.59	0.42	1.60	0.379
Smelter workers	29	2.26	4.82	0.25	53.37	
Totle						
Office workers	15	0.35	4.20	0.05	18.85	0.005
Smelter workers	204	1.22	5.20	0.02	69.05	
Working Procedure						
Lixiviate workers	39	1.48	3.13	0.28	69.05	0.000
Extraction workers	18	1.06	3.79	0.14	35.91	
Metathesis workers	14	4.67	8.06	0.21	61.58	
Electrolysis workers	8	11.15	3.13	0.77	35.40	
Ingot casting workers	2	12.80	1.39	10.13	16.17	
Chemical examination workers	8	0.94	5.49	0.09	36.32	

Note. GM: geometric mean; GSD: geometric standard deviation. MIN: minimum value; MAX: maxmum value.