J Occup Health 2003; 45: 228–230

Short Communication

Biological Monitoring of Indium by Means of Graphite Furnace Atomic Absorption Spectrophotometry in Workers Exposed to Particles of Indium Compounds

Koichi MIYAKI[1], Kanae HOSODA[1], Miyuki HIRATA[2], Akiyo TANAKA[2], Yuji NISHIWAKI[2], Toru TAKEBAYASHI[1], Naohide INOUE[2] and Kazuyuki OMAE[1]

[1]Department of Preventive Medicine and Public Health, School of Medicine, Keio University and
[2]Department of Hygiene, Graduate School of Medical Sciences, Kyushu University, Japan

Key words: Indium, Biological exposure monitoring, Occupational exposure, Graphite furnace atomic absorption spectrophotometry

Since the rapid expansion of III-V semiconductor and liquid crystal display production, the consumption of indium (In) has been increasing. From the mid-1990s, animal experiments have shown that the inhalation or intratracheal instillation of In compounds causes severe lung inflammation[1–7] and mild adverse reproductive effects[8–10]. Although the health effects of In on workers' respiratory and reproductive systems have been unclear to date, assessing the exposure-effect relationships in In-exposed workers is a serious concern, but no information is available on the exposure-effect relationships in workers. This study attempted to estimate the In concentration in biological specimens of In-exposed workers, and to clarify the relationships among them.

Subjects and Methods

The study subjects were 107 workers directly exposed to water-insoluble, partially respirable particles of In compounds and 28 unexposed workers in the same factory who were engaged in factory management jobs. Among the 28 unexposed workers, 4 had past experience of engaging in In-exposed jobs. The mean age of all workers was 35.5 yr (range: 19–59), and the mean exposure length of the 107 workers was 4.56 yr (range: 0.25–17). Whole blood, serum, and spot urine were collected from all of the workers, and the In levels in these specimens were measured with a graphite furnace atomic absorption spectrophotometer (GFAAS, Hitachi Z-5010). The creatinine levels in the urine were determined by Jeffe's method.

For pretreatment of the samples, both a wet-digestion method and a deproteinization method were applied and compared in order to determine the better method. In the wet-digestion method, 100 μl of blood, 200 μl of serum, or 200 μl of urine were taken in a 7 m*l* Teflon tight vial (Tough-tenor, Milestone Inc, USA) with 2 m*l* of 65% ultra-pure nitric acid (Suprapur Nitric Acid, Merck Japan) and digested with a microwave digestion apparatus (EthosPlus/MDR2, Milestone Inc, USA). After digestion, the samples were diluted in to 2 m*l* of distilled water, and introduced into the GFAAS adding 1,000 ppm palladium solution as a matrix modifier. The detection limits of the In in the blood (In-B), In in the serum (In-S), and In in the urine (In-U) (3 times the standard deviation of the blank value) were 0.7, 0.4, and 0.4 $\mu g/l$, respectively. In the deproteinisation method, 200 μl of blood or 200 μl of serum was stirred with 600 μl or 200 μl of 1M ultra-pure nitric acid, centrifuged at 10,000 rpm for 5 min, and the supernatant was introduced into the GFAAS adding 1,000 ppm nickel solution containing 10 mM NH_4 ($EDTA \cdot 2NH_4$) as a matrix modifier. The urine sample was doubly diluted with 0.5% ultra-pure nitric acid, centrifuged at 1,000 rpm for 5 min, and the supernatant was introduced into the GFAAS adding 1,000 ppm palladium solution as a matrix modifier. The detection limits of the In in the blood ($In\text{-}B_{dep}$), In in the serum ($In\text{-}S_{dep}$), and In in the urine ($In\text{-}U_{dep}$) were 0.5, 0.2, and 0.1 $\mu g/l$, respectively.

Results and Discussion

Figure 1a shows a scattergram of the In-B and $In\text{-}B_{dep}$. Although a quite high correlation was found between them (r=0.920), the In-B was ca. 3 times higher than the $In\text{-}B_{dep}$. The relationships between the In-S and $In\text{-}S_{dep}$ and between the In-U and $In\text{-}U_{dep}$ were also similar. These findings indicate that the conditions of deproteinization in this study were inappropriate to assess the In concentrations in the biological specimens. Because the deproteinization method is simple, cheap, and time saving from a practical standpoint, further efforts may be needed to develop suitable deproteinizing conditions.

Table 1 shows representative statistics of the In-B, In-S, In-U and creatinine-adjusted In-U ($In\text{-}U_{adj}$) in 107 current In-exposed workers and in 24 unexposed workers without experience in In-exposed jobs. A half-value of the detection limit was assigned for samples with an In concentration below the detectable limits. Although the In-B, In-S and In-U in 34, 37 and 42 out of the 107 exposed workers and those in 19, 22 and 23 of the 24 unexposed workers were below the detection limits, the exposed workers showed clearly higher In concentrations than the unexposed workers in any of three biological specimens.

Figures 1b-1d show the relationships between In-B and

Received Feb 15, 2003; Accepted May 22, 2003
Correspondence to: K. Omae, Department of Preventive Medicine and Public Health, School of Medicine, Keio University, 35 Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan

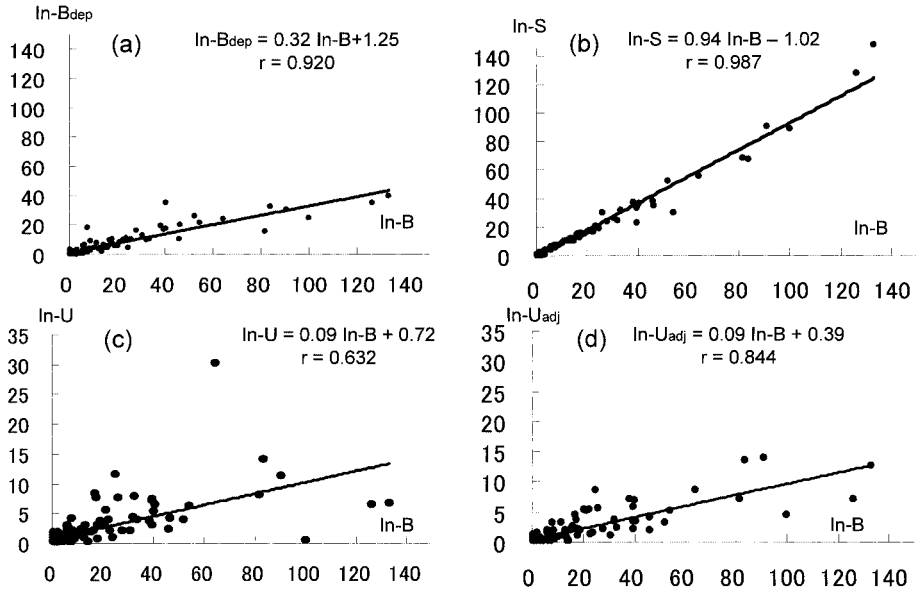

Fig. 1. Relationships between In-B and In-B_{dep}, In-S, In-U or In-U_{adj}. For abbreviations: see text.

Table 1. Representative statistics of biological exposure monitoring indices for In

	AM	GM	GSD	Min.	Median	90th%
Exposed workers (n=107)						
In-B ($\mu g/l$)	16.8	4.09	7.15	<DL	6.44	42.7
In-S ($\mu g/l$)	14.6	2.86	8.81	<DL	5.34	36.1
In-U ($\mu g/l$)	2.45	0.93	4.26	<DL	1.00	6.88
In-U_{adj} ($\mu g/g \cdot Cr$)	2.01	0.82	3.94	<DL	0.73	5.45
Unexposed workers (n=24)*						
In-B	0.57	0.45	1.73	<DL	<DL	0.98
In-S	–	–	–	<DL	<DL	<DL
In-U	–	–	–	<DL	<DL	<DL
In-U_{adj}	–	–	–	<DL	<DL	<DL

*: Four subjects were excluded because of past experience in an In-exposed job. For abbreviations: see text. AM, GM, GSD: arithmetic mean, geometric mean, geometric standard deviation. DL: detection limit. 0.7 $\mu g/l$ for In-B, 0.4 $\mu g/l$ for In-S and 0.4 $\mu g/l$ for In-U.

In-S, In-B and In-U, and In-B and In-U_{adj}. In-B was very closely correlated with In-S (r=0.987, Fig. 1b). The single regression coefficient of 0.94 between them suggests that In may be homogeneously distributed in the blood. In-B was also highly correlated with both In-U (r=0.632, Fig. 1c) and In-U_{adj} (r=0.844, Fig. 1d), which indicates the usefulness of both In-U and In-U_{adj} as biological monitoring indices. When the data with In below the detection limits were excluded and reanalyzed, the correlation coefficients between In-B and In-S, In-B and In-U, and In-B and In-U_{adj} were 0.985, 0.468 and 0.764, respectively. Compared to In-U, In-U_{adj} seems to be a better index because the creatinine adjustment for the urine concentration generated a narrower variation in values and higher correlation with In-B.

In conclusion, In-B, In-S and In-U_{adj} pretreated by the wet-digestion method and determined by GFAAS are useful indices as a biological exposure index of In. When wide variation and the lower concentration of In-U_{adj} are taken into consideration, In-B or In-S may be a more informative index. It will be necessary to use a more sensitive method for the In determination, if the exposure-effect and exposure-response relationships are clarified and the concentrations of In around or below the detection limits are crucial for the health risk assessment.

References

1) ME Blazka, D Dixon, E Haskins and GJ Rosenthal: Pulmonary toxicity to intratracheally administered indium trichloride in Fischer 344 rats. Fundam Appl Toxicol 22, 231–239 (1994)
2) ME Blazka, JS Tepper, D Dixon, DW Winsett, RW O'Connor and MI Luster: Pulmonary response of Fisher 344 rats to acute nose-only inhalation of indium trichloride. Environ Res 67, 68–83 (1994)
3) A Tanaka, A Hisanaga, M Hirata, M Omura, Y Makita, N Inoue and N Ishinishi: Chronic toxicity of indium arsenide and indium phosphide to the lung of hamsters. Fukuoka Acta Med 87, 108–115 (1996)
4) A Tanaka, M Hirata, M Omura, M Zhao, Y Makita, K Yamazaki, N Inoue and K Gotoh: Comparative study of the toxic effects of gallium arsenide, indium arsenide and arsenic trioxide following intratracheal instillations to the lung of Syrian golden hamsters. Fukuoka Acta Med 91, 21–33 (2000)
5) I Kabe, K Omae, H Nakashima, T Nomiyama, T Uemura, K Hosoda, C Ishizuka, K Yamazaki and H Sakurai: In vitro solubility and in vivo toxicity of indium phosphide. J Occup Health 38, 6–12 (1996)
6) T Uemura, K Oda, K Omae, T Takebayashi, T Nomiyama, C Ishizuka, K Hosoda, H Sakurai, K Yamazaki and I Kabe: Effects of intratracheally administered indium phosphide on male Fischer 344 rats. J Occup Health 39, 205–210 (1997)
7) K Oda: Toxicity of a low level of Indium Phosphide (InP) in rats after intratracheal instillation. Indust Health 35, 61–68 (1997)
8) RE Chapin, WH Martha, ES Hunter, BJ Davis, BJ Collins and AC Lockhart: The reproductive and developmental toxicity of indium in the Swiss mouse. Fundam Appl Toxicol 27, 140–148 (1995)
9) M Omura, A Tanaka, M Hirata, M Zhao, Y Makita, N Inoue, K Gotoh and N Ishinishi: Testicular toxicity of gallium arsenide, indium arsenide, and arsenic oxide in rats by repetitive intratracheal instillation. Fundam Appl Toxicol 32, 72–78 (1996)
10) M Omura, K Yamazaki, A Tanaka, M Hirata, Y Makita and N Inoue: Changes in the testicular damage caused by indium arsenide and indium phosphide in hamsters during two years after intratracheal instillations. J Occup Health 42, 196–204 (2000)