An Approach for Bio-monitoring Exposure to Cadmium Hydroxide in Nickel-Cadmium Battery Factory Workers: Impact of Cadmium Levels in Air and Exposure Period on Urinary Cadmium Excretion

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ABSTRACT

The impact of cadmium (Cd) contents in air (CdA) and length of exposure on urinary cadmium (CdU), urinary β2 microglobulin (β2-MGU) and serum β2 microglobulin (β2-MGS) was examined in Cd workers.

Regression analysis between CdA and CdU for short-term (≤ 6 months) workers (Group A, n=126) showed linearity following an equation y = 0.180x+3.72, r=0.944. In long-term (>6 months) workers (Group B, n=348), the relationship was divided into two linear segments described by the equations y = 0.107x+6.24, r=0.698 (designated as group B-1: low risk workers exposed to ≤30 μg/m³ CdA) and y = 0.314x+26.8, r=0.984 (Group B-2: high risk workers exposed to >30 μg/m³ CdA). In these equations x is CdA in μg/m³ and y represents CdU, in μg/l. A nine-month follow-up survey of β2-MGU and β2-MGS on new Cd operators under 5-20 μg/m³ CdA (n=14) showed high volatility increase of β2-MGU and significant increase of β2-MGS.

The lower slope in groups A and B-1 suggest Cd deposition in the liver or kidney. The higher slope in B-2 suggests saturation of binding sites and Cd overflow into urine. It can be concluded that CdU of short-term or low risk workers does not reflect CdA so remarkably as high risk workers. When industrial hygienists assess the initial contact to Cd in low CdA condition, they should be aware of β2-MGU volatility increase and significant increase of β2-MGS.

INTRODUCTION

Cadmium (Cd) is widely used in the manufacturing of rechargeable nickel-cadmium (Ni-Cd) batteries. These batteries are cost-effective and well suited for high power applications, having larger cycle lives and excellent low- and high temperature performance than other chemical systems [1].

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However, Cd is also a well known, extremely toxic metal found in contaminated food and water, tobacco, and industrial fumes and dusts that has no known essential function in humans but is an important toxicological factor in a large number of health conditions [2-5].

The main route of Cd exposure in industrial settings is via inhalation of cadmium hydroxide, Cd(OH)₂, which is utilized as negative electrode in Ni-Cd batteries [6,7] or cadmium sulfide (CdS) powder, used as pigment [8,9]. The absorbed Cd reaches the bloodstream and is widely distributed in the body. The liver and renal cortex are the major organs in which it accumulates and urine is the main route of Cd excretion [10]. The hepatic and renal concentrations may decrease subsequent to renal damage and increased leakage of bound Cd into the urine [11].

In this study, we studied 474 workers divided into two subgroups: (A) Short-term workers who have been working in a Ni-Cd battery manufacturing factory ≤ 6 months and (B) Workers with >6 months on the job, correlating their urinary cadmium (CdU) to the Cd contents in air (CdA) of their workplace. A nine-month follow-up survey of urinary β-2-microglobulin (β2-MGU) and serum β-2-microglobulin (β2-MGS) was also conducted on 14 subjects of new Cd operator in 5-20 μg/m³ Cd A.

It is universally recognized that the best predictive indicators of Cd exposure and its health effects are measurements of Cd in biological fluids, especially urine and blood, CdU and CdB, respectively. Of the two, CdU is conventionally used to determine body burden of Cd in workers without kidney disease and CdB is conventionally used to monitor recent or current Cd exposure [12,13]. β2-MGU and β2-MGS are used as indicator of early tubular dysfunction of Cd exposed subjects [9].

The use of CdU, β2-MGU and β2-MGS to establish the relationship between the degree and duration of occupational exposure to Cd has not been fully studied. For that reason, the aim of the present study was to examine the impact of CdA and the length of exposure on CdU, β2-MGU and β2-MGS in workers exposed to cadmium hydroxide dust in a Ni-Cd battery-manufacturing factory and its relationship to Cd accumulation and overflow into urine.

MATERIALS and METHODS

Subjects

Urine samples for CdU determination were collected from 474 female subjects ages 18 – 28 years working at a rechargeable Ni-Cd battery manufacturing facility. The workers were exposed to dust containing cadmium hydroxide. From the total, 126 subjects had less than six months on the job, constituting group A (short-term workers). The remaining 348 workers have been there for >6 months and formed group B, long-term workers. A nine-month follow-up survey of β2-MGU and β2-MGS was also conducted on 14 new Cd operators. Informed consent of all participants and their legally authorized representatives was obtained. They agree to the purpose of this study and were informed that their samples will never be used other than the purpose of this study.

Serum was separated from the whole blood by centrifugation. The urine and serum samples were frozen and stored at −20°C until analysis.

Air sampling

The low-volume air sampler model L-30 (Shibata Scientific Co. Ltd) and glass fiber filters used to collect air samples have been described in a previous paper [9].

Air samples from the factory were collected at a speed of 30 L/min at a height of 150 cm from the ground, which is the average level of the mouth of an adult Japanese. The samples were bubbled thorough 0.1 M HNO₃ and then subject to Cd analysis. The average CdA exposure level was calculated over the course of an 8-hour work shift or 8-hour time weighted averages (TWA).

Cd, β2-MGU and β2-MGS determination

CdA was determined by means of a Hitachi Z-5700 graphite furnace atomic absorption spectrometer (Tokyo, Japan) and the urinary levels were determined with an AAS-180-50, Atomic Absorption Spectrometer, also from Hitachi. β2-MGU and β2-MGS were measured by the commercial radioimmunoassay method.

Statistical analysis

All the data are expresses as means ± SD. The regression analysis was performed with the statistical analysis software StatView for windows Version 5.0 (SAS Institute Inc). Statistical differences of β2-MGU and β2-MGS were examined by paired Student’s t test.

RESULTS

Figure 1 shows the strong linear relationship found between CdA and CdU in the short-term exposed workers, group A. As shown in regression
Figure 1 Relationship between cadmium in air (CdA) and urinary cadmium (CdU) in subjects of group A (n=126). Symbols and vertical bars represent the mean ± SD of CdU within the distribution range of CdA indicated by x-axis.

Figure 2 Relationship between cadmium in air (CdA) and urinary cadmium (CdU) in subjects of group B (n=348). Symbols and vertical bars represent the mean ± SD of CdU within the distribution range of CdA indicated by x-axis. Superimposed arrow indicates the gap that divides the two segments of the plot.

Analysis of this figure, the plot follows the equation $y = 0.180x + 3.72$ ($r=0.944$), where $x$ is CdA (μg/m³) and $y$ is CdU (μg/l).

Figure 2 shows the relationship between CdA and CdU in the long-term exposed workers, group B. As shown in this figure, there is also a strong linear relationship between CdA and CdU but the plot shows a gap of about 28 μg/l in the CdU values at CdA = 30 μg/m³, as indicated by a double arrow in Fig. 2. Regression analysis yielded the equations $y = 0.107x+6.24$ ($r=0.698$) for segment B-1 (designated as group B-1: low risk workers exposed to CdA of ≤30μg/m³) and $y = 0.314x+26.8$ ($r=0.984$) for segment B-2 (Group B-2: high risk workers exposed to CdA of >30μg/m³).

Figure 3 shows the β2-MGU trend in a nine-month follow-up survey of new Cd operators. As shown in this figure, β2-MGU of new Cd operators indicates high volatility increases with wide SD ranges with no statistical difference after the start of their works were confirmed.

Figure 4 shows the β2-MGS trend in a nine-
Figure 3 Trend of β2-MGU in a nine-month follow-up survey of new Cd operators (n=14). Symbols and vertical bars represent the mean ± SD at 0 (before engagement), 1, 3 and 9 month(s) after engagement in Cd working.

Figure 4 Trend of β2-MGS in a nine-month follow-up survey of new Cd operators (n=14). Symbols and vertical bars represent the mean ± SD at 0 (before engagement), 1, 3 and 9 month(s) after engagement in Cd working. *p<0.01 and **p<0.001: significant difference from before engagement.

month follow-up survey of new Cd operators. As shown in this figure, β2-MGS of new Cd operators shows significant increase after the start of their works.

DISCUSSION

Cd is an extremely toxic metal commonly found in recent industrial workplaces. Industrial hygienists have designed guidelines for safe levels of exposure in the workplace. The American Conference of Governmental Industrial Hygienist (ACGIH) set the threshold limit value (TLV-TWA) for Cd at 0.01 mg/m³ and the Japanese Society for Occupational Health set the occupational exposure limit (OEL) at 0.05 mg/m³.

The observed CdA <0.08 mg/m³ in this study mostly overlapped in the range of the limit between TLV-TWA and OEL, with a slight excess of OEL. This level of exposure is lower than that reported by Kawasaki et al. [9] for workers of a Cd pigment factory where CdA was in the 0.024 — 1.221 mg/m³.
range. They also found that CdU was a suitable way to assess Cd exposure in high CdA condition [9], and other study also reported that CdU to be a convenient way to monitor the level of exposure to Cd [13].

As regards CdU, Yassin et al. reported a geometric mean of 0.30 µg/l (0.28 µg/g creatinine) with distribution range of 0.01 to 15.57 µg/l for U.S. workers [14] and Minoia et al. gave a reference value in the 0.38-1.34 µg/l range for Italian population [15]. The y-intercept from the A, B-1 and B-2 plots exceed those reference values and confirm that the three study groups were exposed to Cd.

Animal experiments have shown that absorbed Cd is initially bound to albumin in blood plasma and then reaches the liver, where metallothionein (MT), an intracellular binding protein is synthesized to protect against Cd toxicity by forming a non-toxic Cd-MT complex [16].

Eventually this complex is released into the circulation, crossing the glomerular filtration barrier where is endocytosed by the apical megalin receptor in the proximal tubule cells [17]. Free Cd, the toxic form, is then released from the endosomes and contributes to Cd-induced renal damage. As the proximal tubule is the main site of Cd re-absorption and more than 90% of the filtrated Cd is reabsorbed along this segment [18], chronic exposure causes renal dysfunction in humans [19,20] and animals [21,22]. Cd accumulates in the kidney cortex over the entire lifetime with biological half-life of 30 years in human [23].

The relationship between CdA and CdU seen in group A shows a uniform linear relationship but in group B is discontinuous, where an upward break occurs when CdA reaches 30 µg/m². In the upper segment the slope becomes steeper. The slopes of groups A (0.180) and group B-1 (0.107) are 42.6-66.0 % smaller than that of group B-2 (0.314). The lower slope of groups A and B-1 suggest that most of the absorbed Cd is being accumulated in the liver or kidney, which accounts for a low CdU excretion rate. The break observed in group B at CdA ~ 30 µg/m² and higher slope of B-2 suggest that the amount of accumulated Cd in liver or kidney exceeded their capacity and that Cd is overflowing into urine, thus increasing the CdU excretion rate.

As the recent occupational hygienic conditions of the major companies are greatly improved in developed countries, the future main target for the prevention of occupational Cd exposure will be to detect early signals of long-term exposure to low CdA or initial Cd exposure of new employees. The United States Occupational Safety and Health Ad-

ministration (OSHA) rule for Cd requires a program of periodic biological monitoring of CdB, CdU, β2-MGU and β2-MGS for workers exposed to CdA for 30 or more days per year at levels >2.5 µg/m². There are significant relationships among these three items and CdU is a useful mean biological monitoring of assessing Cd exposure particularly in high CdA conditions [9]. Although β2-MGU of new Cd operators showed no significant increase in a nine-month follow-up survey of the present study, β2-MGS showed significant increase. Both high volatility increase of β2-MGU and significant increase of β2-MGS can be a good indicator to assess their initial contact to Cd in low CdA condition.

From experiments in vitro and in vivo we know that MT protects against Cd toxicity by binding to MT and that the resulting Cd-MT complex is nontoxic when stored intracellularly. Renal cell injury occurs when a critical concentration of Cd is exceeded via a mechanism that is still unknown, although it has been suggested that an unidentified form of Cd other than Cd-Mt becomes available [24]. High volatility increase of β2-MGU and significant increase of β2-MGS in new Cd operators observed in this study may suggest the early renal reaction to free Cd in advance of forming Cd-MT complex and excessive production of β2-MG.

When conventional CdU is utilized as predictor to assess Cd exposure in occupational settings and Cd exposure is indicated by the detection of CdU above a reference range, industrial hygienists should be aware that the CdU of short-term workers and of long-term low risk workers such as the subjects in our groups A and B-1 do not reflect CdA as well as long-term high risk workers (B-2 subjects). The possibility that Cd accumulation in the liver or kidney potentially occurs before a high rate CdU excretion is observed must be given full consideration and additional renal function tests including β2-MGU and β2-MGS are necessary for the early detection of deleterious effects of long-term exposure to low levels of CdA or in cases of early exposure of recent employees.

REFERENCES


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