Cadmium in human lung tissue

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Received August 30, 1989 / Accepted June 27, 1990

Summary. In 101 unselected autopsies, cadmium (Cd) in lung tissue was analyzed by means of flameless atomic absorption spectrometry (AAS). The subjects originated from Bochum (BO), Dortmund (DO), and neighbouring cities in the Ruhr District (BO/DO) as well as from Muenster (MS) and vicinity. The sample included eight persons who had died from bronchial carcinoma. The Cd concentration in lung tissue (CdL) did not show a significant age-dependency. There was only a slight increase of CdL in the age around 50. For males, the median CdL value was found to be 1.32 µg/g dry wt in the age group from 20–45, 1.48 µg/g dry wt from 45–65, and 0.64 µg/g dry wt > 65 (the corresponding means and standard deviations were 1.48 ± 1.22, 1.73 ± 1.42, and 1.18 ± 1.27 µg/g dry wt). CdL in men was twice that in women. There were no differences between the two regions (BO/DO:MS) examined. CdL of the bronchial carcinoma cases were mostly clearly above the expected level, often similar to the Cr and Ni concentration of the same specimens. Besides the amount of inhaled metal aerosols, insufficient lung clearance may play a leading role for their retention in lung parenchyma. However, with regard to the determination of causality between uptake and disease the data are difficult to interpret, in our study due to a lack of enough consistent and reliable data on occupation, environment, and smoking habits, and in general due to a lot of variables which, until now, cannot be sufficiently quantified.

Key words: Cadmium concentration – Lung tissue – Atomic absorption spectrometry – Bronchial carcinoma

Introduction

Tissue residues of toxic/carcinogenic material in target organs (where uptake and/or deposition take place) serve as an indicator for a preceding total load and are used as important additional information for the determination of causality between exposition and disease. Lung cancer is the most important occupational and environmental cancer with regard to its frequency and severeness. Therefore, the content of more or less evidently carcinogenic substances (e.g. asbestos, certain compounds of chromium, nickel, arsenic, cadmium etc.) in samples of lung tissues obtained at autopsy is worth determining.

Relevant human exposure to cadmium (Cd) occurs mainly through the oral intake of food and drinking water and, in certain situations, through the inhalation of Cd-contaminated air; uptake by inhalation is significantly increased through smoking. Furthermore, the air of industrial and residential areas is constantly polluted by at least small amounts of Cd, and this metal gets partly accumulated in the lung. Therefore, the question arises when and to what extent a given Cd concentration in lung tissue (CdL) is increased with regard to the average of a comparable population, i.e. how much do the observed values differ from the population mean and what do these differences mean.

Materials and methods

In unselected autopsies at the Institute of Pathology of the University Hospital Bergmannsheil Bochum (n = 34) and at the Institute of Legal Medicine of the city of Dortmund (n = 7) from 1984 to 1988, Cd in lung tissue was analysed. The same had been done before with lung tissue specimens (n = 60) obtained from the Institute of Pathology of the University of Muenster (MS) [13]. The subjects were adults from the catchment area of the university hospitals who had died from various causes, including eight persons who had died from bronchial carcinoma (Table 2). Partly we obtained a crude history of smoking habits, occupation, and place of residence. Bochum (BO) and Dortmund (DO) are part of the Ruhr District which is defined as a particularly polluted area (NW-Belastungsgebiet); the cases from there have been combined into a common sample (BO/DO). The tissue specimens were always taken from the same part of the lung, i.e. a particular area at the lateral base of the right upper lobe. In all BO/DO-cases three similar specimens were each removed from this narrow organ region to be able to calculate the intraindividual variation of the pulmonary Cd concentration. In seven of the MS-cases two similar specimens were taken for the
same reason. Mostly the chromium (Cr) and nickel (Ni) concentration of the lung tissue specimens had been determined in earlier series, too [11].

The Cd concentration was determined by means of flameless atomic absorption spectrometry (AAS) after lyophilisation, wet ashing under pressure, chelating, and extraction. We have described our analytical method elsewhere in full detail, including the very strict precautions for preventing metal contamination during specimen collection and processing [13, 20, 21]. Four specimens of 100 mg are analysed from each tissue, applying standard additions before ashing. After the sample solution is distributed to two AAS cups, each part specimen is measured four times. The final concentration is calculated with the corresponding mean values and linear correlation and stated in ng/g freeze-dried tissue. Measured or mean values that vary considerably are rejected. The following are exclusion criteria: coefficient of variability (CV) ≥ 5% with four measured values, as well as r = 0.997 or CV of the slope and the intercept of the regression line together ≥ 10%.

The precision was established by random control determinations after the specimens had been stored for several weeks. The analytical characteristics were:

- detection limit (threefold variation from blind values of several days): 2 ng/g dry wt;
- precision (n = 9): 4.5%;
- accuracy (checked with NBS SRM 1577 bovine liver) (n = 9): 447 ± 20 ng/g dry wt (certification value: 440 ± 60 ng/g).

For the statistical analysis of the data, we used the same methods and techniques as in earlier investigations on the tissue content of Cr and Ni in lung [12], especially ln-transformed data for a better approach to a normal distribution.

Using a simple statistical variance component model, it was possible to estimate the magnitudes of the interindividual and the intra-individual variabilities, and hence get the reliability of the concentration data.

Taking into account that a similar age-dependent behavior of the CdL should be expected as in kidney cortex (CdKc), we fitted parallel age-dependent parabolic curves in a covariance model separately for the four different sex/region combinations to the mean ln(CdL) within each analysed lung.

Results

The measurement values of the whole series are plotted in Fig. 1, median and range of several subgroups as well as some individual values are shown in Tables 1 and 2. The under 20 age range (Table 1a, b) and the bronchial carcinoma cases (Table 1c, d) were calculated separately. One of the carcinoma cases had an extremely high Cd value (Table 1d) and had to be regarded as an outlier.

The variance component analysis showed that the ln-transformed Cd values have an intra-individual variance of 0.064 and an inter-individual variance of 1.692. If the cases with an age below 20 as well as those with bronchial carcinoma are removed, these values are still 0.063 and 1.058. Hence, the variation of the ln-transformed CdL is explained by the intra-individual variance only by less than 5%, i.e., we have a reliability of more than 95%.

There is a slight increase of the mean CdL at the age of around 50. However, in the analysis of covariance model described above, no significant age dependency can be found: the curvature for male [ln(CdL) = −1.699 + 0.0668 age − 0.000629 age²] is significant only to a P-value of 0.105. This value increases if non-parallel curves are allowed in the model. Furthermore, no difference is found between the CdL of the subjects from the Ruhr District (BO/DO) and of those from Muenster (MS) and surroundings. On the other hand, differences between men and women are obvious (P = 0.003). Parallel parabolic curves separately fitted for men and women are shown in Fig. 1 (note that their height differs by an amount of e^0.667, this means that CdL for men is 1.95 times as high as for women). The factor as well as Fig. 1 should be handled carefully due to the lack of significance of the parameters used in the estimation.

In our opinion, in the present situation it is only reasonable to give some descriptive values for several subgroups, especially for age classes (Table 1). For reasons of robustness, we used the median and the range.

In the analysis of covariance above, the bronchial carcinoma cases have not been used. It is noteworthy, however, that their ln(CdL) with one exception are higher than to be expected with regard to the fitted curves of Fig. 1 (Table 2).