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Beryllium in exhaled breath condensate as a biomarker of occupational exposure in a primary aluminum production plant

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ABSTRACT

Objective: Low beryllium exposure can induce pulmonary granulomatosis, so called berylliosis. For occupational health monitoring, it is more relevant to assess the internal dose of Be received by the lungs than urinary or atmospheric Be. Exhaled breath condensate (EBC) is a matrix collected non-invasively that derives from the airway lining fluid. EBC beryllium (Be) levels were evaluated as a marker of occupational exposure in a primary aluminum production plant.
Methods: We collected urine and EBC from controls and workers recently exposed to beryllium in the pot room and the anode repair sectors, and calculated a cumulative beryllium exposure index (CBEI) summing the number of years of employment in each task and multiplying by the estimated average beryllium exposure for the task. Concentrations of beryllium and aluminum were measured in EBC (Be-EBC and Al-EBC) and in urine (Be-U and Al-U) by ICP-MS.
Results and conclusion: We have shown that it was possible to measure Be and Al in workers' EBC. Compared with controls and after adjustment for smoking status, levels of Be-EBC and Al-EBC were higher in pot room workers and exposed subjects, respectively. Due to its relationship with CBEI, but not with Be-U, it appears that Be-EBC could be a promising marker of occupational exposure and provide additional toxicokinetic information in occupational health studies.

Abbreviations: ANSES, Agency for Food, Environmental and Occupational Health & Safety; Al, aluminium; ACGIH, American Conference of Governmental Industrial Hygienists; ANCOVA, analysis of covariance; ANOVA, analysis of variance; Be, beryllium; CHRU, Centre Hospitalier Régional Universitaire de Lille; CBEI, cumulative beryllium exposure index; EBC, exhaled breath condensate; FVC, forced vital capacity; ICP-MS, inductively coupled plasma mass spectrometer; IQR, interquartile range; LOQ, limit of quantification; MMEF, maximal mid-expiratory flow; FEV1, maximum forced expiratory volume in a second; RSD, relative standard deviation; sd, standard deviation; SE, standard error; TURBO-DECCS, Transportable Unit for Research on Biomarkers Obtained from Disposable Exhaled Condensate Collection Systems.

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1. Introduction

The number of workers exposed to beryllium (Be) is estimated to be around 67,000 in Europe (Kauppinen et al., 2000). Beryllium exposure can cause diseases that can be severe such as lung cancer (Boffetta et al., 2012) and berylliosis, a pulmonary granulomatosis that requires a prior sensitization phase (Marchand-Adam et al., 2005; Marchand-Adam and Valeyre, 2005). Owing to the occurrence of berylliosis cases after relatively low occupational exposure (Kelleher et al., 2001; Taiwo et al., 2010), the occupational exposure limit of $2\,\mu g\,m^{-3}$ set by the French circular of 12 January 1995 has recently been the subject of revision (Borak, 2006). The American Conference of Governmental Industrial Hygienists (ACGIH) recently proposed a decrease in its present limit value from $2\,\mu g\,m^{-3}$ to $0.05\,\mu g\,m^{-3}$ (American Conference of Governmental Industrial Hygienists, 2009) while the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) proposed a lower value of $0.01\,\mu g\,m^{-3}$ to avoid any risk of sensitization (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail, 2010).

Despite its benchmark status, beryllium measurements in urine remain a controversial biomarker of exposure due to the variability of its excretion depending on the chemical form to which people are exposed (WHO-CICAD, 2001). Moreover, urinary levels of unexposed subjects vary widely and, according to Apostoli and Schaller (2001), further studies are needed to determine a reliable biological exposure index for urinary beryllium. Kent et al. (2001) suggested that level of particles smaller than 3.5 microns is a more relevant measure of exposure as it represents actually deposit in the alveolar compartment and predicts incidence of sensitization or onset of chronic beryllium disease.

Since inhalation is the main route of absorption of beryllium, we thought it important to develop a more reliable biological exposure index that would offer direct insight into the lungs' Be burden and better link it to occupational exposure *via* inhalation.

Exhaled breath condensate (EBC) is a matrix that can be sampled non-invasively and has the potential to reflect occupational exposure to metallic particles (Chérot-Kornobis et al., 2012). Indeed, particles that reach the alveolar compartment can be collected in the EBC according to the bronchiole fluid film burst model of Johnson and Morawska (2009). Several studies in different occupational activities have already used the EBC as a matrix reflecting the occupational exposure to inhaled metal dust. Goldoni and coworkers have shown the potential usefulness of EBC to complete and integrate biomonitoring and health surveillance procedures among workers exposed to cobalt and tungsten (Goldoni et al., 2004). Hoffmeyer and colleagues have demonstrated the usefulness of EBC for the medical surveillance of welders, assaying metals such as nickel, iron, and chromium (Hoffmeyer et al., 2012). We have previously shown that manganese in EBC is a biomarker of occupational exposure in welders using the Metal Inert Gas process (Hulo et al., 2014). To the best of our knowledge, no studies have been published assaying Be in EBC or using it as a biomarker of occupational exposure. The aim of this study was therefore to evaluate, in an exposed-control study, the feasibility of assaying Be in EBC at the same time as aluminum (Al), and to relate their concentrations in EBC to the atmospheric metal concentrations in an occupational exposure setting within a primary aluminum production plant.

2. Materials and methods

2.1. Study population

We conducted an exposed-control study on a population of 30 workers exposed to beryllium within a primary production of aluminum and 21 unexposed control subjects at the same time from the tertiary sector of the same plant. We recruited 18 subjects among the 80 pot room workers and 15 from among the 16 welders in the anode repair sector between December 2010 and December 2011. Included exposed subjects were those whose last exposure to Be was less than 8 days ago. One pot room worker and 2 welders were thus excluded because their last exposure to Be was outside this time limit, hence we included 17 pot room workers and 13 welders.

Aluminum is produced between a cathode and an anode by electrolytic reduction in order to extract the metal from alumina which contains variable concentrations of Be. Various metal species are produced, such as difluoride Be, Al, sodium, and fluor during the redox reaction, and thus released into the atmosphere of the pot room. The strict internal regulations of the company require workers in the pot room to wear powered air purifying respirators with a gas and dust filter unit.

Beryllium is gradually enriched in the electrolysis bath after each production cycle and is deposited on the anodes. An anode is a carbon block suspended above the electrolysis bath within a metal structure consisting of six mild steel feet connected to an aluminum rod by a steel shaped spider. Owing to their wear during use, anodes must be regularly repaired by welders. First, they have to disconnect the feet from the steel shaped spider by air arc gouging that produce a large amount of metal dust. They then weld new feet to the spider and, if necessary a new aluminum rod, using the MIG welding process. Welders often had to reload the different pieces with metal as mild steel or aluminum. Therefore, the dust produced during these operations contains the same Be compounds as those released to the atmosphere in the pot room. According to the strict internal regulation of the company, welders must wear powered air purifying respirators with a gas and dust filter unit during these operations.

Controls were enrolled at the same plant than the exposed subjects and had no current or previous Be exposure. We excluded all controls working in the vicinity of the pot room or anode repair sectors or at other locations that would potentially expose them to Be.

This study was performed after approval of the company's Committee of Health and Safety Working Conditions. All subjects were fully informed about the aims of the study, and gave their prior, free and informed consent. Details that might disclose the identity of the subjects under study were omitted. This study was approved by the French data protection commission (Commission Nationale de l'Informatique et des Libertés, reference number 1390323) and the Advisory Committee on Protection of Persons in Biomedical Research (reference number 2009-A00518-49).

2.2. Study design

All subjects answered a questionnaire in two parts:

- The first part of the questionnaire concerned their background, in particular their respiratory health, including any respiratory symptoms, smoking habits, and tobacco consumption. The questionnaire on respiratory symptoms was that used by the European Community for coal and steel on respiratory symptoms (Minette, 1989).
- The second part of the questionnaire concerned occupational history, particularly the type and the duration of the tasks performed that may result in exposure to beryllium.

We made the following measurements and collected the following samples from workers during a single workday at occupational