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Mutation Research 586 (2005) 102–114

Genetic Toxicology and Environmental Mutagenesis

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Occupational exposure to mercury vapour on genotoxicity and DNA repair

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Received 22 November 2004; received in revised form 3 June 2005; accepted 8 June 2005

Abstract

We have conducted a population study to investigate whether current occupational exposure to mercury can cause genotoxicity and can affect DNA repair efficiency. Blood samples from 25 exposed workers and 50 matched controls were investigated for the expression of genotoxicity. The data indicate that mercury exposure did not cause any significant differences between the workers and controls in the baseline levels of DNA strand breaks (as measured by the alkaline version of the single cell gel electrophoresis [SCGE] assay) or sister chromatid exchanges (SCE). However, the exposure produced elevated average DNA tails length in the SCGE assay and frequency of chromosome aberrations. In the studies, isolated lymphocytes were exposed to 6 J/m^2 UV-C light or 2 Gy dose of X-rays in a challenge assay and repair of the induced DNA damage was evaluated using the SCGE assay. Results from the UV-light challenge assay showed no difference between the workers and controls in the expression of DNA strand breaks after exposure followed by incubation in the absence or presence of the cellular mitogen (phytohemagglutinin, PHA). No difference in DNA strand breaks between the workers and controls was seen immediately after the X-ray challenge, either. However, significant differences were observed in cells that were incubated for 2 h with and without phytohemagglutinin. Data from the X-rays challenge assay were further used to calculate indices that indicate DNA repair efficiency. Results show that the repair efficiencies for the workers (69.7% and 83.9% in un-stimulated and stimulated lymphocytes, respectively) were significantly lower than that of matched controls (85.7% and 90.4%, respectively). In addition, the repair efficiency showed a consistent and significant decrease with the duration of occupational exposure to mercury (from 75.7% for <10 years employment, to 65.1% for 11–20 years and to 64.1% for 21–35 years) associated with increase of cytogenetic damage. Our study suggests that the occupational exposure to mercury did not cause a direct genotoxicity but caused significant deficiency in DNA repair. Our observations are consistent with previous studies using the standard chromosome aberration

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doi:10.1016/j.mrgentox.2005.06.009

assay to show that exposure to hazardous environmental agents can cause deficiency in DNA repair. Therefore, these affected individuals may have exposure-related increase of health risk from continued exposure and in combination with exposure to other genotoxic agents.
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Keywords: Mercury exposure; Genotoxicity; Sister chromatid exchanges; Chromosome aberrations; DNA strand breaks; Single cell gel electrophoresis assay; DNA repair; Challenge assay

1. Introduction

It has been well documented that exposure to high concentrations of mercury can cause damage to the nervous system, immune system, kidney and liver in humans [1–4]. Some evidence indicates that mercury can cause toxicity to developing embryos because mercury ions can penetrate the blood-placenta barrier to reach the embryos [5]. For example, environmental disasters have been caused by the exposure to mercury in Japan and in Iraq [6]. Despite the knowledge of hazards from mercury, human populations continue to be exposed to mercury. A major concern is whether the current occupational exposure to mercury is safe for workers or not. The mechanisms of toxicity of mercury have been investigated but not well characterized yet. Heavy metals such as mercury do not usually induce obvious genotoxic effects but interfere with numerous cellular activities such as cellular repair enzymes [7] to enhance genotoxicity [8–10]. It is possible that prolonged exposure to low concentrations of mercury in occupational conditions may cause problems associated to enzymatic activity of the DNA repair that can result in a long-term health consequences.

For population studies, the challenge cytogenetic assay is useful for investigating the phenomenon of exposure-induced DNA repair deficiencies [11–13]. In the assay, lymphocytes from workers and matched controls are irradiated in vitro with X-rays to challenge the cells to repair the induced DNA damage. Increase of chromosome aberrations in the workers over the controls is used to indicate the induction of DNA repair deficiency from the occupational exposure. Using the challenge assay, populations exposed to cigarette smoke, uranium, butadiene, pesticides and styrene were shown to have DNA repair deficiency [11–16]. On the other hand, workers exposed to very low concentrations of benzene and mothers exposed to environmental pollutants did not have DNA repair deficiency [6,17]. Recently, the assay was used to validate that certain variant DNA repair genes (e.g. *XRCC1* and *XPA*, respectively) are defective in the base excision and the nucleotide excision repair pathways [15]. In our study, we propose to use a modified version of the challenge assay. Instead of using chromosome aberrations, we used a DNA strand break assay, the single cell gel electrophoresis assay (SCGE) which is a sensitive method for detecting DNA strand breaks and alkali labile sites [18,19]. These abnormalities are readily induced in cells from exposure to ionizing radiations such as X- or γ-rays and correlate well with the chromosomal damage observed in the first mitotic division [21]. Non-ionizing radiation like UV-C (maximum absorption for DNA molecule is observed at 260 nm wavelength) causes pyrimidine dimers and 4,6-pyrimidine photoproducts. Therefore, UV irradiation itself does not induce DNA strand breaks directly but when cells are incubated due to excision process pyrimidine dimmers are converted into strand breaks that are detectable by the SCGE assay. In our previous study [22,23], we showed no significant increase of DNA strand break immediately after exposure to UV-C, but time-dependent increase of strand breaks was shown during the post-exposure incubation up to 1.5 h. Those studies also indicated that addition of the phytohemagglutinin (PHA) mitogen to the culture medium caused significant acceleration of the repair of strand breaks that were induced by UV-light and other genotoxic agents.

The aim of this study was to find out whether occupational exposure to low concentrations of mercury vapour might be associated with the expression of genotoxicity and with defective DNA repair capacity. For the evaluation of DNA repair capacity, cells were exposed to UV-light or X-rays and the irradiated cells were analyzed for the presence of DNA strand breaks immediately after exposure and after the incubation of the irradiated cells in culture medium with and without the presence of PHA.

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