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Association between exposure to nitric oxide and changes in select molecular markers of health among men in the gold jewelry manufacturing industry

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Abstract

Gold jewelry workers are occupationally exposed to nitric oxide (NO) during the purification of gold. The present study involves the evaluations of chromosome aberrations (CA), micronucleus (MN) and comet assay in lymphocytes and identifies the influence of polymorphisms in DNA repair genes (*XRCC1*^{280}Arg/His, *XRCC1*^{399}Arg/Gln) among the gold jewelry workers occupationally exposed to nitric oxide (NO). Among the 84 samples undertaken for study, the non-exposed (categorized based only on age being group I <35years; group II ≥35 years) and exposed subjects (categorized based on age and work duration) constituted 42 subjects each. With increase duration of years of exposure, an increased level of chromosomal damage was observed. Likewise, a higher degree of chromosomal damage and MN was observed in exposed subjects of group II with a total CA of 8.07 ± 3.29 and MN of 10.61 ± 2.25 when compared to group I. Significant increases were also indicated with the overall CA frequency for the exposed subjects for chromatid, chromosome type aberrations and the MN/1000 binucleated cells in peripheral lymphocytes ($p < 0.05$) in comparison with non-exposed. The analysis of mean tail length of comet assay shows the DNA damage among the group II exposed subjects exhibits higher degree of chromosomal damage, indicating chronic exposure of NO causes the genetic modification, largely influenced by the polymorphic genotypes *XRCC1*^{280}Arg/His ($p < 0.001$) and *XRCC1*^{399}Arg/Gln (0.524). In conclusion, this result of work provides evidence for an apparent genotoxic effect associated with

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NO exposure. Our result reinforces the higher sensitivity of cytogenetic assays for the biomonitoring of occupationally exposed populations. So there is a strong need to educate those who work with potentially hazardous heavy metals about their adverse effects and highlight the importance of using protective measures.

Keywords: Nitric oxide; Jewelry workers; Chromosomal aberrations; Comet assay; XRCC1

1. Introduction

Workers involved with jewelry manufacturing are exposed to a number of potentially hazardous substances such as metals (silver, gold, beryllium, zinc, antimony, aluminum, lead, arsenic, cadmium, mercury, and copper), various dusts (talc, containing asbestos, and silica; aluminum oxide and other abrasives), solvents (toluene and xylene), organic (trichloroethylene) and inorganic (nitric acid) chemicals every day [1]. For making jewelry and coins, gold and its alloys are commonly used, during this process, aqua regia solution containing concentrated nitric acid and hydrochloric acid dissolves the gold and forms Au^{3+} ions whereas chloride ions from hydrochloric acid react with gold to produce chloaurate anions; further oxidation takes place on the solution and gold is dissolved. During this process, NO radical (NO•) is produced. The NO radical produced in the cell mediates a diverse array of actions such as vasodilatation, neurotransmission and iron metabolism [2]. Effects due to NO on cells are reported to be dose-dependent leading to cytostatic and its effects by inhibition of DNA synthesis, damage to mitochondria, loss of cell membrane integrity, apoptosis, changes in cell cycle distribution, occurrence of DNA single strand breaks (SSB) and DNA–protein cross-link [3–5]. Prolonged exposure of nucleic acids to NO/reactive nitrogen species (RNS) results in deamination by converting Cytidine (C) to Uridine (U), Guanosine (G) to Xanthosine (X), and methyl Cytidine (C) to 5-Methyluridine (T) [6].

The current occupational and safety and health administration (OSHA) standard for NO is 25 ppm (30 mg/m^3) of air, averages over an 8 h work shift (Baur and Barbinova, 2005). The concentration ratio of NO and oxygen (O_2) primarily determines the fate of NO. NO can react with O_2 and subsequently induce DNA damage by deaminating the DNA bases, resulting in mutation [5,7]. Hogg et al., 1996 and Li and Hotchkiss, 1995 reported NO as a tumor initiating agent known for its involvement in cancer development and reviews indicate increased level of NO identified in the patients of oral cancer, head and neck cancer, chronic obstructive pulmonary disease, arthritic disorders, asthma and type 1 diabetes mellitus [1,10].

Molecular studies shows insight into the risk of cancer associated with genotoxic damage influenced by individual susceptibility, thus making them relevant for hazard exposure identification and risk assessment in order to prevent future cancers. The scaffolding protein XRCC1 (X-ray repair cross-complementing group 1) plays an important part in base excision repair (BER) [11] by promoting an efficient SSB repair; after removal of damaged bases by DNA glycosylases. XRCC1 mediates protein–protein interactions with DNA ligase III, PARP (polynucleotide kinase/phosphatase-poly ADP-ribose polymerase) [12]. Two coding region polymorphisms that result in amino acid changes in *XRCC1*^{280}Arg/His and *XRCC1*^{399}Arg/Gln of the *XRCC1* gene indicating either reductions in DNA repair capacity or the fidelity of DNA repair was studied by Shen et al., 1998 and Svilar et al., 2011.

The identification of chromosomal aberrations (CA) in human peripheral blood lymphocyte culture (PBLC) is recognized as a valuable biomarker in monitoring environmental toxicants, and is the only method which has been internationally standardized and validated [15]. Micronucleus (MN) test has been used for over 20 years in order to measure the occupational exposure to toxic agents among the human population exposed to industrial toxicants. This cytogenetic test assesses the MN originating from chromosome fragments or whole chromosomes that are not included in the main daughter nuclei during nuclear division [16]. Comet assay, on the other hand, is a rapid, simple, and sensitive technique for measuring and analyzing DNA breakage in individual cells [17]. This single cell gel electrophoresis (SCGE) technique has found numerous applications in genetic toxicology, environmental biomonitoring and clinical investigations [18] and is extensively used in studies involving genotoxicity of