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Chromosomal aberrations and oxidative DNA adduct 8-hydroxy-2-deoxyguanosine as biomarkers of radiotoxicity in radiation workers

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ABSTRACT

Background: There are evidences of association between occupational radiation exposure, cytogenetic alterations and the increase in cancer rates. It is known that the probability of carcinogenesis is greater in populations exposed to radiation, since ionizing radiation can raise the frequency of chromosomal aberration and spontaneous mutations.

Objective: Our purpose was to assess the role of chromosomal aberrations and oxidative DNA adduct 8-hydroxy-2-deoxyguanosine (8-OHdG) as biomarkers of radiation injury in individuals occupationally exposed to ionizing radiation.

Subjects: and Methods: Blood samples were collected from 60 radiation workers and 30 healthy volunteers age and sex matched as control group who had never worked in radiation-related jobs. Chromosomal aberrations in peripheral blood lymphocytes were assayed by conventional cytogenetic technique and serum levels of 8-OHdG was measured by enzyme linked immunossorbent assay (ELISA).

Results: The incidence of all types of chromosomal aberrations was significantly higher in all exposed groups than in controls with the highest rate of chromosomal aberrations in the industrial radiographers. Serum 8-OHdG in all radiation workers was significantly higher than in control group. There was a significant higher values among industrial radiographers compared to diagnostic radiologists or radiotherapists. Significantly lower mean corpuscular volume (M.C.V) was found among radiation workers versus the controls reflecting erythrocyte microcytosis.

Conclusions: Scoring of chromosome aberrations such as breaks, fragments and dicentrics is a reliable method to detect previous exposure to ionizing radiation. This type of monitoring may be used as a biological dosimeter instead of physical dosimetry.8-OHdG is a useful oxidative DNA marker among radiation workers and those exposed to environmental carcinogens.

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1. Introduction

Humans are naturally exposed to ionizing radiation from cosmic rays, and artificially through diagnostic procedures, medical treatments or occupationally during work shifts. It is well known that ionizing radiation produces DNA damage through different mechanisms: by loss of bases, single-strand breaks, double strand breaks, and damage to purine and pyrimidine bases. This early damage may lead to chromosomal aberrations and thus to increased risk of mutagenesis and carcinogenesis (Martínez, Coleman, Romero-Talamás, & Frías, 2010). It is considered that no dose of ionizing radiation exposure is safe. However, once the accurate absorbed dose is estimated, one can be given appropriate medical care and the severe consequences can be minimized. Though several accurate physical dose estimation modalities exist, it is essential to estimate the absorbed dose in biological system taking into account the individual variation in radiation response, so as to plan suitable medical care. Over the last several decades, lots of efforts have been taken to design a rapid and easy biological dosimeter requiring minimum invasive procedures. The metaphase chromosomal aberration assay in human lymphocytes still remains the gold standard for radiation biodosimetry (Agrawala, Adhikari, & Chaudhury, 2010).

Cytogenetic studies in radiation workers have demonstrated an increase in the frequency of chromosomal aberrations in comparison to non-exposed individuals. These chromosomal aberrations are the result of an erroneous repair of the DNA lesions produced by radiation (Ballardi et al., 2007; Kasuba, Rozgaj, & Jazbec, 2008).

Ionizing radiation is a well-established carcinogen due to the resulting oxidative damage, and the molecule most often affected is DNA. Interactions of ionizing radiation with DNA consist of the direct ionization of DNA (direct effect) and its reaction with surrounding water molecules (the indirect effect), followed by DNA destruction by the induced radicals (•OH, e−• and, to much lesser extent, H•) (Karbownik & Reiter, 2000). Generally among nucleic acid components, guanine is the most susceptible DNA target for oxidative reactions mediated by •OH (Shirazi, Ghobadi, & Ghazi-Khansari, 2007). The modified base 8-hydroxydeoxyguanosine (8-OHdG), an oxidative adduct form of deoxyguanosine, is considered a sensitive marker of DNA damage due to a hydroxyl radical attack at the C8 of guanine. Such damage is usually successfully repaired, but if unrepaired, the presence of 8-OHdG in DNA templates may cause the miscoded incorporation of nucleotides in the replicated strand, which may contribute to the development of cancer (Sperati et al., 1999).

The objective of the present study was to assess the role of chromosomal aberrations and oxidative DNA adduct 8-hydroxy-2-deoxyguanosine (8-OHdG) as biomarkers of radiation injury in individuals occupationally exposed to ionizing radiation.

2. Subjects and methods

This study included 60 subjects occupationally exposed to ionizing radiation (radiation workers), their mean age was (35.0 ± 6.67) years. Thirty healthy volunteers age and sex matched who had never worked in radiation-related jobs served as control group, their mean age was (33.53 ± 7.27) years. Radiation workers were divided into three groups according to their job title at the time of blood collection, as follow:

- Radiotherapy group (n = 20) (working on linear accelerator), their mean age and working period was 36.25 ± 6.70 and 11 ± 7.60 years respectively.
- Diagnostic radiology group (n = 20) (using medical diagnostic X-ray machine), their mean age and working period was 31.65 ± 7.58 and 9 ± 6.90 years respectively.
- Industrial radiographers group (n = 20) (using Iridium 192 as a gamma source for radiography), their mean age and working period was 37.10 ± 4.61 and 8.15 ± 4.59 years respectively.

The annual accumulated dose was measured during the person's entire working time using personal dosimeters (film badge and pocket dosimeter). The mean dose was 2.93 ± 1.91 and ranged from 1.5 to 4.5 mSv/year in diagnostic radiology group and 3.13 ± 1.46 and ranged from 1.5 to 6 mSv/year in radiotherapy group. Regarding industrial radiographers group, the mean dose was 5.46 ± 2.35 and ranged from 4 to 13.5 mSv/year.

All subjects were interviewed and completed a questionnaire including demographic data, smoking habit, lifestyles, medical records and radiation exposure history. A written consent for participating in the study was taken according to the declaration of Helsinki and approved by the ethical committee of the Medical Research Institute. The radiation workers were selected from Diagnostic Radiology Department in Medical Research Institute, radiotherapists in Ayadi Al-Mostakbal Oncology Center and industrial radiographers in petroleum sector who followed up in Hematology Department in Medical Research Institute.

None of the study individuals reported alcohol consumption or the presence of known inherited genetic disorders or chronic diseases. None of them received chemotherapeutic drugs or subjected to ionizing radiation for diagnostic or therapeutic purposes in the six months previous to blood collection.

2.1. *Cytogenetic method*

Venous blood samples were collected into heparinised tubes. Lymphocytes cultures were set up within 24 h of sampling according to the conventional method (Sharma & Sharma, 1980). Whole blood cultures were established by placing 0.5 ml of PRMI medium supplemented with 20% fetal calf serum and 1.5% phytohaemagglutinin. Cultures were incubated in the dark at 37 °C for 48 h. Colchicine [0.1 mg/ml] was added for the last 2 h of incubation to arrest the cells at metaphases. Cells were incubated with hypotonic KCl [0.075 M] at 37 °C for 10 min and fixed in 4 changes of cold 3:1 methanol/acetic acid. Slides were prepared by the heat drying technique and were stained with aqueous Giemsa solution. One hundred metaphase were analyzed for every participant.