Serum 8-Hydroxy-2′-Deoxyguanosine Level as a Potential Biomarker of Oxidative DNA Damage Induced by Ionizing Radiation in Human Peripheral Blood

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Abstract

In this study, the effect of ionizing radiation on 8-hydroxy-2′-deoxyguanosine (8-OHdG) in human peripheral blood was investigated. Blood samples were collected from 230 radiation workers and 8 patients who underwent radiotherapy for population study. Blood samples from 2 healthy individuals were irradiated with different X-ray doses for in vitro experiment, and levels of 8-OHdG in serum and cell culture supernatants were assessed by enzyme-linked immunosorbent assay. Observations demonstrated the positive relationships between serum 8-OHdG level and radiation dose and working period were observed, and serum 8-OHdG levels were higher among interventional radiation workers than among other hospital radiation workers. In addition, 8-OHdG yields in supernatants increased, peaked at 3 Gy of radiation dose, and then decreased with further increases in radiation; the dose–response curve obtained fitted a polynomial function. By contrast, a similar trend was not found in radiotherapy patients. The present study suggests that 8-OHdG may be a useful biomarker reflecting oxidative damage among workers occupationally exposed to low-dose radiation.

Introduction

Exposure to ionizing radiation (IR) from natural environment background radiation is inevitable. Interestingly, the annual effective dose produced by artificial radiation sources (eg, nuclear reactors, linear accelerators, X-ray machines) is nearly equal to the total radiation dose obtained from natural sources.[1] With the widespread application of IR in several industries, occupational exposure to low-dose radiation is common; exposure to high-dose radiation within a short time may also occur in the event of radiation accidents. As thus, it is necessary to pay sufficient attention to radiation safety in order to prevent radiation accidents. Ionizing radiation, as a toxicant and carcinogen, can produce reactive oxygen species and cause severe oxidative and DNA damage, such as single- and double-strand breaks, oxidized bases, and DNA–protein cross-links.[2,3] If these damages are not repaired correctly, they may lead to chromosomal aberration (CA), cell death, and increased risk of gene mutation and cancer. Although the International

Commission on Radiological Protection recommends an effective dose limit of 20 mSv per year, averaged over 5 years, with the further provision that the effective dose should not exceed

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50 mSv in any single year,[4] radiation workers remain at high risk.[5,6] Some traditional cytogenetic methods for radiation biodosimetry have been used in radiation accidents, including CA analysis, micronuclei assay, and translocation assay by fluorescence in situ hybridization.[7] Especially, CA assay is considered the "gold standard" for radiation biodosimetry[8,9]; however, it is labor-intensive and time-consuming requiring 72 to 96 hours for dose estimation. Thus, rapid and sensitive methods are needed to monitor the DNA damage induced by IR.

Oxidative damage induced by IR is thought to be critically involved in radiation damage and the hydroxyl radical (HO·) plays an important role in this process.[10,11] The damage-induced HO· is believe to account for two-thirds of all DNA damages caused by X-rays in mammalian cells.[1] The interaction of HO· with the nucleobases leads to the generation of oxidation products, such as 8-hydroxy-2′-deoxyguanosine (8-OHdG) or 8-oxo-7,8-dihydro-2′-deoxyguanosine which is generated from the keto–enol tautomerism of 8-OHdG. They are usually used for the same compound and considered typical markers of oxidative damage due to HO· attack at C8 of guanine.[10] Such damage may result in miscoded incorporation of nucleotides in the replicated strand if it cannot be repaired, and may contribute to the development of cancer.[12] As an internationally recognized biomarker of DNA oxidative damage, 8-OHdG is stabilized in the body; it is not affected by the diet or cellular renewal and it can be induced by various xenobiotics.[13-15] Several studies have also suggested that 8-OHdG is linked to many kinds of diseases, from tumors, cardiovascular disease to diabetes.[16-18] However, to the best of our knowledge, few previous studies have evaluated the impact of IR on 8-OHdG levels.

In this study, the relation between IR exposure and 8-OHdG levels in serum was preliminarily examined by population study and in vitro experiment. The purpose is to evaluate the serum 8-OHdG levels of individuals exposed to IR, including occupational low-dose radiation and high-dose radiation, to improve the awareness of the biological effect of radiation and explore the feasibility of serum 8-OHdG as a biomarker of IR.

Materials and Methods

Study Population and Ethics Statement

Radiation workers. The present study recruited 230 age- and sex-matched radiation workers (108 males and 122 females), 31 to 51 years of age, from hospitals in Zhengzhou, the capital of Henan Province, China. The occupational exposure of the participants to IR ranged from 1 to 26 years. All radiation workers were divided into 4 groups according their job at the time of blood collection, including diagnostic radiology (n = 75), radiotherapy (n = 60), nuclear medicine (n = 41), and interventional radiology (n = 54) group. All participants were interviewed by professional interviewers and completed a questionnaire regarding demographic data, occupational history, working period, medical history, and individual history of disease. Exclusion criteria included chronic disease, occupational exposure to other toxic agents or carcinogens except IR, chemotherapy, antioxidant therapy, or exposure to IR for medical treatment in the 12 months immediately before blood collection.

Radiotherapy patients. Eight patients (3 males and 5 females), 44 to 78 years old, were chosen from the Department of Radiation Oncology of The Fifth Affiliated Hospital of Zhengzhou University in Henan, China. The inclusion criterion was as follows: patients with solid tumors (such as thoracic neoplasms and abdominal neoplasms), who received radiotherapy only. Depending on the phases of the patients' treatment, venous blood samples were drawn before and after each radiotherapy course, once a week, 5 times in total. All blood samples were divided into 5 dose groups with cumulative doses of 0, 10, 20, 30, and 40 Gy. Using a self-control method, serum 8-OHdG level of each patient was measured at the baseline and post-treatment with radiation.

The study was conducted at Henan Institute of Occupational Medicine (HIOM). The scope of the study was explained to each patient, and the Ethics Committee of HIOM approved of all experiments (201702, March 20, 2017). After obtaining informed consents, approximately 3 mL of peripheral blood was collected from each patient using vacutainer tubes.

In Vitro Experiment for Acute Exposure

Blood samples were collected in vacutainer tubes with EDTA dipotassium salt from the median cubital vein of 2 healthy donors (1 male and 1 female), 25 to 35 years old, who did not smoke or drink alcohol and had no history of clinical diseases or exposure to radiation or other xenobiotics. The donors did not use medications and had no disease at the time of blood collection. Written consent was obtained from each donor.

Thirty-six milliliters of whole blood samples was obtained from each donor and divided into 3 groups. In each group, 6 samples were processed and irradiated with X-rays from a medical linear accelerator (Elakta, Stockholm, Sweden) at the Department of Radiation Oncology of The Fifth Affiliated Hospital of Zhengzhou University in Henan, China, at a dose rate of 2 Gy/min, over an area of 10 cm ×10 cm, at room temperature. Group 1 was the sham group, and groups 2, 3, 4, 5, and 6 were exposed to 0.25, 0.5, 1, 3, and 8 Gy radiation, respectively. Two milliliters of whole blood were inoculated on 6 mL PRMI-1640 medium (Gibco, Grand Island, New York) supplemented with 10% fetal bovine serum (Thermo, Beijing, China) and 0.2% gentamycin (80 mg/mL, Sinopharm, Beijing, China). The cultures were incubated in the dark at 37 for 24, 48, and 72 hours, respectively. Culture supernatants were then separated, and 8-OHdG concentrations were detective by enzyme-linked immunosorbent assay (ELISA) method.

Sample Preparation

Venous blood samples were obtained using disposable and sterile needles and collected into vacuum tubes without anticoagulant. The blood samples were coded and transported to the laboratory, where they were allowed to rest for 30 minutes at room temperature. Collected blood or the cultures were centrifuged at $3000 \times g$ for 10 minutes, after which the serum or supernatant was transferred to 1.5 mL labeled centrifuge tubes and stored at -80 until analysis.

Individual Monitoring of Occupational External Exposure

According to GBZ 128-2016 Specifications for Individual Monitoring of Occupational External Exposure, a national standard enacted by the National Health and Family Planning Commission of the People's Republic of China, the personnel effective dose per year was monitored using a thermoluminescent dosimeter (PTW-Freiburg, Freiburg im Breisgau, Germany). The personal external radiation dosages were measured 4 times in a year and the duration of monitoring was 3 months per period. After elimination of distorted data, the annual effective dose was calculated as follows:

$$H_p(10) = (\bar{x} - \bar{x}_0) \times Cf$$

where $H_p(10), \bar{x}, \bar{x}_0,$ and Cf indicate individual penetrating dose equivalent (mSv), the mean of the background reading (mGy), the mean of the measured value (mGy), and the calibration coefficient of the thermoluminescent dosimeter (mSv), respectively.

Serum and Supernatant 8-OHdG Measurement

Serum or culture supernatants 8-OHdG levels were measured by human 8-hydroxydeoxyguanosine ELISA kit (CUSABIO, Wuhan, China) according to the manufacturer's instruction. This assay employs the competitive inhibition enzyme immunoassay technique. In brief, samples were thawed at room temperature and centrifuged at $13.4 \times g$ for 3 minutes before use. Then, 50 µL of the standard or a sample per well was added into each well of a 96-well microplate that had been coated with the 8-OHdG-specific antibody; 50 µL of horseradish peroxidase (HRP) conjugate was also added to each well. The mixtures were combined well and incubated at 37 for 60 minutes. After aspirating and washing each well 3 times with 200 µL of wash buffer ($1\times$) per well, 50 µL of substrate A and 50 µL of substrate B were added to each well. Incubation at 37 for 15 minutes in humid and dark incubator followed. Then, 50 µL of stop solution was added to each well and the optical density of each well was determined within 10 minutes, using a microplate reader (Autobio, Zhengzhou, China) set to 450 nm, with the correction wavelength set to 600 to 630 nm. The detection range was 2 to 800 ng/mL. The assay was performed in technical duplicate.

Statistical Analysis

Statistical analysis was performed using SPSS version 17, and data were presented as mean (standard deviation [SD]). Pearson χ^2 test was used to assess differences between groups in the distribution of categorical variables, and Student t test or 1-way analysis of variance (ANOVA) was used to assess differences between groups for continuous variances. Pearson correlation coefficients were calculated to evaluate the association between relevant parameters. The influence of age, gender, type of job, occupation, annual effective dose, and working period on serum 8-OHdG level was examined by multiple linear regression analysis. All statistical tests were based on a 2-sided probability, with significance level of .05.

Results

Characteristic of Radiation Workers

The mean age, working period, and personal effective dose of the 230 radiation workers recruited to this study were 37.90 (4.45) years, 9.87 (5.54) years, and 0.53 (0.35) mSv, respectively. The demographic characteristics of exposed workers grouped by job classification were provided in Table 1. No significant differences were observed between 4 groups in terms of mean age ($P = .705$), gender ($P = .704$), and whole white blood cell count ($P = .088$). As expected, significant differences were found between groups in terms of working period and radiation dose. Among the participants, workers in the interventional radiology and radiotherapy groups, respectively, received the highest (0.75 [0.44] mSv) and the lowest (0.41 [0.20] mSv) radiation doses.

Serum 8-OHdG Level of Radiation Workers

Serum 8-OHdG measurements were summarized in Table 2 and Figure 1. No statistically significant differences in terms of age, gender, and occupation groups ($P = .098, .735, .680,$ respectively) were observed. Significant differences were found in different job classifications. The mean serum 8-OHdG levels of the diagnostic radiology, radiotherapy, nuclear medicine, and interventional radiology groups were 80.93 (23.71), 91.44 (32.98), 95.63 (34.83), and 120.29 (63.88) ng/mL, respectively. Moreover, serum 8-OHdG levels were significantly higher in the interventional radiology group than that in the diagnostic radiology, radiotherapy, and nuclear medicine groups ($P < .05$). Significant differences were observed between the diagnostic radiology and nuclear medicine groups ($P < .05$). Nonsignificant differences in serum 8-OHdG levels were observed between the radiotherapy and diagnostic radiology groups, as well as between the radiotherapy and nuclear medicine groups ($P = .055, .599,$ respectively).

As shown in Figure 1, the personal effective dose and working period were divided into several subgroups, and statistically significant differences were observed between different doses and working period groups ($P < .05$). In terms of effective dose

Table 1. Characteristics and Hematological Indices of Radiation Workers in All Studied Groups.

Characteristics	Diagnostic Radiology	Radiotherapy	Nuclear Medicine	Interventional Radiology	χ^2/F Value	P Value
N	75	60	41	54		
Age, year					0.467	.705
Mean (SD)	37.48 (3.16)	38.35 (5.46)	38.12 (5.89)	37.80 (3.43)		
Range	31-45	31-51	31-51	32-45		
Gender, n (%)					1.409	.704
Male	37 (49.33)	28 (46.67)	16 (39.02)	27 (50.00)		
Female	38 (50.67)	32 (53.33)	25 (60.98)	27 (50.00)		
Radiation dose (mSv)					19.178	<.05
Mean (SD)	0.44 (0.23)	0.41 (0.20)	0.56 (0.42)	0.75 (0.44)		
Range	0.09-1.79	0.21-1.61	0.11-2.21	0.19-2.61		
Work period (year)					9.758	<.05
Mean (SD)	12.28 (4.91)	9.22 (5.85)	8.93 (6.28)	7.94 (4.20)		
Range	3-26	2-26	2-24	1-17		
WBCs (10^9/L)					2.209	.088
Mean (SD)	5.84 (1.20)	5.55 (1.53)	5.45 (1.21)	5.28 (1.00)		
Range	4.0-8.8	2.8-10.7	3.2-7.2	2.8-10.7		

Abbreviation: SD, standard deviation; WBCs, white blood cells.

Table 2. Serum 8-OHdG Levels of 230 Radiation Workers.

Characteristics	N (%)	8-OHdG Level	F Value	P Value
Age, year				
<35	58 (25.22)	86.89 (28.11)	2.349	.098
35-40	105 (45.65)	95.26 (45.23)		
≥40	67 (29.13)	103.44 (48.34)		
Gender				
Male	108 (46.96)	93.96 (39.19)	−0.339	.735
Female	122 (53.04)	96.92 (45.98)		
Occupation				
Physician	127 (55.22)	98.80 (49.07)	0.387	.680
Technician	45 (19.56)	90.23 (35.35)		
Nurse	58 (25.22)	92.48 (32.21)		
Job classification				
Diagnostic radiology	75 (32.61)	80.93 (23.71)	9.071	<.001
Radiotherapy	60 (26.09)	91.44 (32.98)		
Nuclear medicine	41 (17.83)	95.63 (34.83)		
Interventional radiology	54 (23.47)	120.29 (63.88)		

Abbreviation: 8-OHdG, 8-hydroxy-2′-deoxyguanosine.

(Figure 1A), the mean serum 8-OHdG level in the ≥1 mSv group was 131.42 (770.23) ng/mL, which was significantly higher than that in the <0.5 mSv and 0.5 to 1 mSv groups (87.91 [32.33] and 101.32 [46.89] ng/mL, respectively; $P < .05$). In addition, for working period (Figure 1B), the serum 8-OHdG levels of patients in 4 groups were 76.70 (25.77), 97.89 (45.57), 99.18 (39.72), and 100.32 (49.09) ng/mL, respectively. Student t test revealed that the 8-OHdG level of workers with seniority of approximately 5, 10, and over 15 years were higher than those who worked less than 5 years ($P < .05$).

To evaluate the relationship between serum 8-OHdG level and effective dose or working period, the correlation analysis was performed. Results showed that a significant positive correlation between serum 8-OHdG levels and personal effective dose or working period ($r = 0.300, 0.142, P < .05$). This funding revealed that serum 8-OHdG levels increased with increasing radiation dose and working period. Multiple regression analysis was applied to estimate the influences of age, gender, occupation, job classification, annual effective dose, and working period on serum 8-OHdG levels (Table 3). Job classification, dose (mSv), and working period (year) partly affected serum 8-OHdG levels ($R^2 = 0.200, P < .001$). These findings contrast the result that age, gender, and occupation had no relation with 8-OHdG levels ($P = .588, .140, .878$, respectively).

In Vitro Irradiation Experiment

The serum 8-OHdG levels observed after irradiation in cultured human whole blood samples were demonstrated in Figure 2A. Exposure of blood samples to radiation doses of 0, 0.25, 0.5, 1, 3, and 8 Gy caused respective increases of 9.40 (2.16), 10.38 (2.47), 11.26 (2.24), 11.81 (2.89), 12.72 (2.89), and 10.70 (1.96) ng/mL 8-OHdG level in the culture supernatants. Analysis of variance indicated that the impact of radiation dose on 8-OHdG level was extremely significant ($P < .05$), while incubation time exerted no such significant effect ($P = .978$; Figure 2B). The 8-OHdG levels significantly increased after 0.5, 1, and 3 Gy irradiation compared to that in the sham control group ($P < .05$). An inflection point was noted between exposure to 3 Gy of radiation and serum 8-OHdG concentration; specifically, 8-OHdG production in supernatants linearly increased and peaked upon exposure to 3 Gy of radiation and then moderately decreased. As illustrated in Figure 2C, the radiation dose–response curve was fitted to a polynomial function at the dose range of 0 to 8 Gy, because the R^2 value of this equation, which represents the goodness of fit, was better than that of the linear curve.
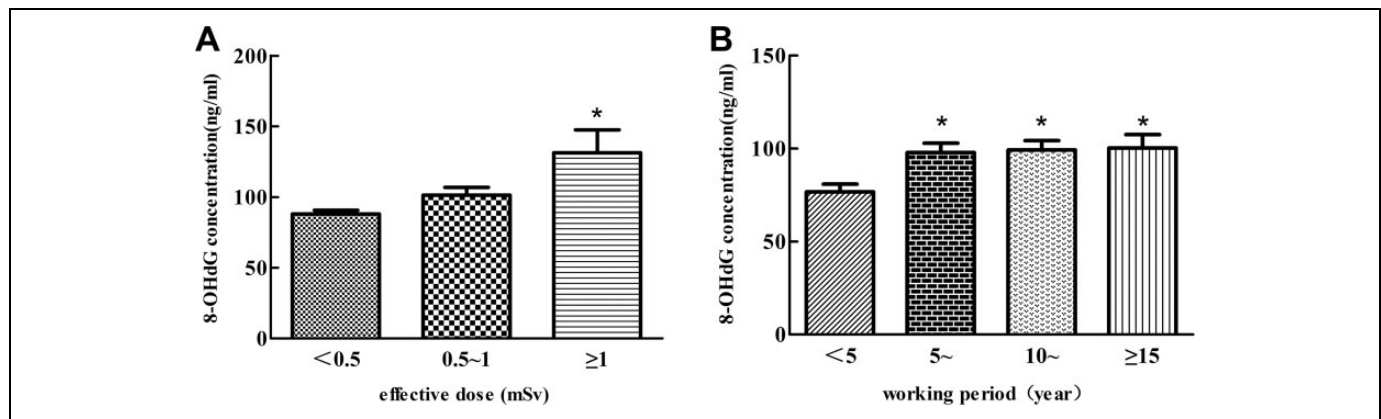
Figure 1. Effects of (A) effective dose of radiation and (B) working period on serum 8-OHdG levels. Bars indicate the mean $\pm$ SEM of serum 8-OHdG level in each group. *P < .05 compared to the first group (<0.5 mSv group of dose and <5 year group of working period). 8-OHdG indicates 8-hydroxy-2′-deoxyguanosine; SEM, standard error of the mean.

Table 3. Linear Regression Analysis of Impact Factors Influencing Serum 8-OHdG Levels in Radiation Workers.

Variables	b	S_b	b'	t Value	P Value
Gender	8.021	5.419	0.094	1.480	.140
Age	0.359	0.661	0.037	0.543	.588
Occupation	0.489	3.177	0.010	0.154	.878
Working period	12.037	3.591	0.248	3.352	.001
Job classification	12.908	2.666	0.349	4.841	.000
Personal effective dose	9.852	4.389	0.148	2.245	.026

Abbreviations: 8-OHdG, 8-hydroxy-2′-deoxyguanosine; b, unstandardized coefficients; S_b, standardized error; b', standardized coefficients.

Serum 8-OHdG Level of Patients Undergoing Radiotherapy

The mean (SD) of serum 8-OHdG levels in 8 patients with cancer before treatment was 196.71 (42.66) ng/mL; by comparison, mean serum 8-OHdG levels recorded after radiotherapy with cumulative dose of 10, 20, 30, and 40 Gy were 178.91 (53.18), 187.54 (33.00), 192.08 (58.61), and 147.21 (35.77) ng/mL, respectively. Serum 8-OHdG levels decreased from 196.71 to 147.21 ng/mL after 4 treatment sessions but increased slightly with radiotherapy of cumulative doses of 10, 20, and 30 Gy. What made us regrettable was that no significant difference in serum 8-OHdG levels was observed between different therapeutic dose groups, and a linear correlation between the accumulated exposure dose and 8-OHdG was not found.

Discussion

Oxidative DNA damage is linked to prolonged and acute exposure to xenobiotics. Over the past few years, many plausible findings have been published, including the relation between 8-OHdG level and IR, benzene, fine particulates, ethylbenzene, and heavy metals such as chromium.[19-21] Several studies[22,23] have reported that the increased 8-OHdG levels are associated with occupational low-dose radiation exposure. One research[23]

found significantly higher 8-OHdG levels in urine among pilots occupationally exposed to cosmic radiation compared to that of the unexposed group. Differences of CA frequency and 8-OHdG level have also been noted between the human serum of healthy individuals and radiation workers, and positive correlations between serum 8-OHdG levels and age, working period, annual accumulated dose, and CA frequency have been found.[12] However, due to the small sample size and excluded interventional radiologists, some limitations in that study have been identified. On the contrary, other researchers held a contrary view that the 8-OHdG levels are lower in individuals subjected to prolonged exposure to radiation than in healthy persons, due to the enhanced DNA repair capacity.[24,25]

The current study revealed that serum 8-OHdG levels are higher among interventional radiologists than other radiation workers, which reflects a higher degree of oxidative DNA damage in the former's bodies. Earlier research indicated that DNA damage increases with increasing radiation dose, thereby demonstrating a clear dose–response relationship.[26,27] This situation can be explained by the fact that radio intervention operation was a fluoroscopically guided procedure, which requires workers to maintain close contact with X-rays for a long time. Thus, interventional radiologists may occupationally receive the highest individual radiation dose. This postulation in accordance with the data obtained from our individual radiation dose monitoring. Moreover, with increasing number of working years, serum 8-OHdG levels presented an increasing tendency in this study, likely because the accumulative dose of radiation workers increases along with the extension of their working period.

Researchers have been pointed out that age and gender affect radiosensitivity and the generation of DNA damage[28-30] and that genetic instability increases with age in human cells as well. For example, a positive correlation has been noted between sister chromatid exchange frequency and age of patients.[6] However, these findings remain controversial as other authors did not find a relationship between radiosensitivity and age or gender.[31] Some researchers have found an association between 8-OHdG level and age or gender,[32,33] while others have not.[34] In
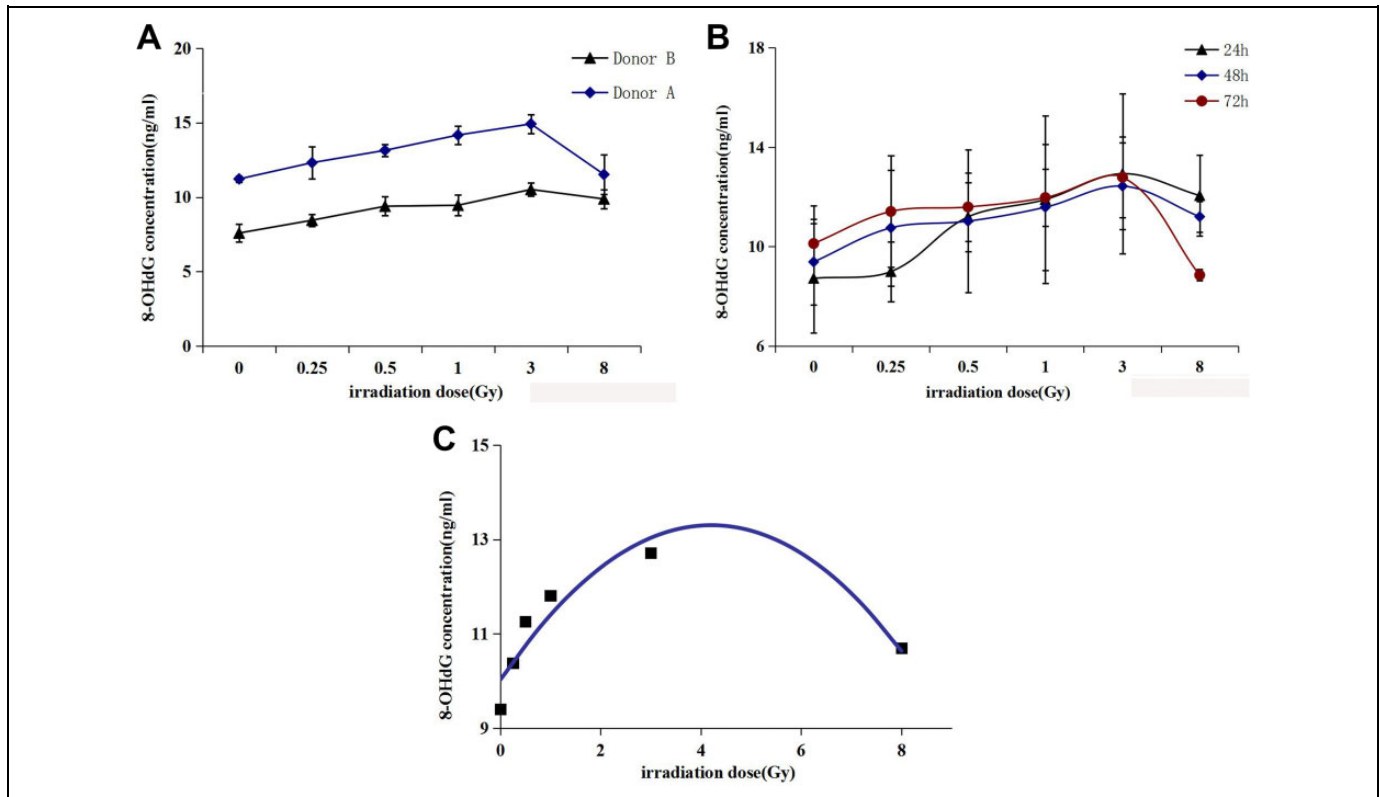
Figure 2. A, 8-Hydroxy-2′-deoxyguanosine levels of 2 blood donors following irradiation with different doses (0, 0.25, 0.5, 1, 3, and 8 Gy). Values are expressed as the mean $\pm$ SEM. B, 8-OHdG levels in blood cultures incubated for 24, 48, and 72 hours. C, The radiation dose–response curve was made by plotting 8-OHdG level against the radiation absorbed dose (0, 0.25, 0.5, 1, 3, and 8 Gy). The data were fitted to polynomial function at the dose range of 0 to 8 Gy, and the following equation was obtained: $Y = -0.185D^2 + 1.557D + 10.02$ ($R^2 = 0.863$). 8-OHdG indicates 8-hydroxy-2′-deoxyguanosine; SEM, standard error of the mean.

this study, neither population studies nor in vitro assay revealed evidence that age and gender directly impacted 8-OHdG levels in human blood was found.

We evaluated the changes in 8-OHdG levels brought about by acute exposure to large doses of radiation. According to our in vitro experiment, 8-OHdG levels in culture supernatants appeared to be associated with irradiation dose, and the dose–response curve was fitted to polynomial function. We suppose that 8-OHdG levels declined after exposure to over 3 Gy of radiation may be attributed to the high percentage of cell death under high radiation doses. Therefore, as observed by other authors,[26] a threshold dose seems to exist.

Based on our in vitro experiment, we explored serum 8-OHdG levels in individuals exposed to high-dose radiation over a short period of time. Taking the noxious properties of IR into consideration, exposing healthy people to radiation violates ethical principles, so patients with cancer who received radiotherapy were chosen as subjects in this study. Results showed that serum 8-OHdG levels, during and after 4 treatment sessions, were lower than untreatment, though it increased slightly during previous 3 times of treatment sessions (10, 20, and 30 Gy). These finding may be explained from the viewpoint of 3 aspects. On the one hand, living organisms may have a series of defense mechanisms to avoid error and minimize the

accumulation of oxidative DNA damage caused by IR.[35] In addition, DNA damage requires time to repair, so changes in DNA adduct production induced by IR may be more significant in the recovery stage (several days or months) than in the initial period of damage.[36] On the other hand, the fact that 8-OHdG was associated with various cancers, which means patients normally have higher levels of 8-OHdG than healthy people, could be a confounding factor.[37-39] Cancer cells are killed gradually by radiation treatment, which contributes to the decline of serum 8-OHdG levels. Previous research[40] also found that levels of urinary 8-OHdG decline through radiotherapy, and no linear correlation between 8-OHdG and the accumulated dose has been observed. In addition, the biological effects of fractional irradiation are weaker than those induced by a single irradiation at the same dosage.

Although 8-OHdG levels can be detected by several methods,[41] ELISA seems to be the most common method. Some studies,[42,43] however, cast doubt on the technique's sensitivity for detecting 8-OHdG, as several authors insist that ELISA shows high variability, overestimates the true values compared to other methods, and cannot be recommended for accurate quantification of 8-OHdG. Nonetheless, no evidence to entirely rule out the application of the ELISA in 8-OHdG detection has been presented, because, although differences between the

8-OHdG levels detected by different methodshave been observed, the overall trends were similar.[42] In the current study, we chose ELISA to detect 8-OHdG for its specific advantages, which include rapid detection, simple operation, low cost, and suitability to studies with large number of samples, which may be conducive to screening exposed populations for radiological triage.

The strengths of the present study include a relatively large sample size involving the medical industry which has the largest number of radiation workers, and evidence of the feasibility of applying 8-OHdG as a biomarker of oxidative damage induced by IR is presented from the perspectives of chronic low-dose radiation and acute high-dose radiation, through a population study and in vitro experiment. In addition, the self-control method is applied to analyze the impact of radiation serum 8-OHdG levels in patients undergoing radiotherapy, which ensures that evaluation results comparable and authentic. Despite the knowledge gained, however, some limitations of this study should also be noted. Considering the presence of individual differences, the sample size of the in vitro experiment should be enlarged. The states of radiation workers' smoking and alcohol consumption were not determined, and these states may lead to some bias. Several studies assessing the association between 8-OHdG level and smoking or alcohol consumption show somewhat higher 8-OHdG levels among smokers and drinkers compared to those among nonsmokers or drinkers.[44,45]

Conclusion

This study suggests that exposure to IR could lead to oxidative damage, which is characterized by elevated serum 8-OHdG levels. In terms of occupational low-dose radiation, this study selected radiation workers in hospitals as the main objects, and serum 8-OHdG levels were found to be significantly higher in interventional radiology workers, and 8-OHdG levels were related to working period and radiation dose. The association between 8-OHdG level and acute radiation was evaluated in 2 ways. The results of an in vitro experiment showed a dose–response curve fitting a polynomial function, while data from patients who underwent radiotherapy suggested no linear correlation between serum 8-OHdG levels and accumulative radiation dose. Consequently, serum 8-OHdG levels may be applied as a biomarker reflecting oxidative damage among workers occupationally exposed to low-dose radiation. Whether 8-OHdG levels could be used in accidents involving high-dose irradiation requires further investigation.

Authors' Note

Yu Gao and Ping Wang contributed equally to this work. Yu Gao and Yumin Lyu conceived and designed the experiments; Ping Wing, Fengling Zhao, and Qiao Zhang conducted the experiments; Yu Gao, Ping Wang, Zhaonan Wang, Jianpo Wang, and Fang Zhao carried out the experiments and performed the data analyses; Lin Han and Jie Li collected and separated the blood samples; Chongbin Tian performed the individual monitoring of external exposure; Yu Gao wrote the manuscript; and Yumin Lyu and Qiao Zhang revised the manuscript.

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