Sperm quality and DNA damage in men from Jilin Province, China, who are occupationally exposed to ionizing radiation

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ABSTRACT. Long-term radiation exposure affects human health. Ionizing radiation has long been known to raise the risk of cancer. In addition to high doses of radiation, low-dose ionizing radiation might increase the risk of cardiovascular disease, lens opacity, and some other non-cancerous diseases. Low- and high-dose exposures to ionizing radiation elicit different signaling events at the molecular level, and may involve different response mechanisms. The health risks arising from exposure to low doses of ionizing radiation should be re-evaluated. Health workers exposed to ionizing radiation experience low-dose radiation and have an increased risk of hematological malignancies. Reproductive function is sensitive to changes in the physical environment, including ionizing radiation. However, data is scarce regarding the association between occupational
radiation exposure and risk to human fertility. Sperm DNA integrity is a functional parameter of male fertility evaluation. Hence, we aimed to report sperm quality and DNA damage in men from Jilin Province, China, who were occupationally exposed to ionizing radiation. Sperm motility and normal morphology were significantly lower in the exposed compared with the non-exposed men. There was no statistically significant difference in sperm concentration between exposed and non-exposed men. The sperm DNA fragmentation index was significantly higher in the exposed than the non-exposed men. Chronic long-term exposure to low doses of ionizing radiation could affect sperm motility, normal morphology, and the sperm DNA fragmentation index in the Chinese population. Sperm quality and DNA integrity are functional parameters that could be used to evaluate occupational exposure to ionizing radiation.

Key words: Sperm DNA damage; Ionizing radiation; Occupational exposure; Sperm parameter

INTRODUCTION

Long-term radiation exposure affects the health of the human body. Late-onset effects of exposure to ionizing radiation on health have been identified by long-term, large-scale epidemiological studies (Kamiya et al., 2015). Ionizing radiation has long been known to raise the risks of cancer (Abbott, 2015). In addition to high doses of radiation, low-dose ionizing radiation (LDIR) might increase the risk of cardiovascular disease, lens opacity, and some other non-cancerous diseases (Hammer et al., 2013; Kamiya et al., 2015; Kreuzer et al., 2015). The authors of previous research have reported that cardiovascular morbidity and mortality may occur decades after ionizing radiation exposure (Yan et al., 2014). The health risks arising from exposure to low doses of ionizing radiation should be re-evaluated (El-Saghire et al., 2013).

Although the response to ionizing radiation-induced DNA damage involves special mechanisms of DNA repair (Yang et al., 2014b), long-term radiation exposure and the late-onset effects of exposure should be taken seriously. Previous studies have shown that health workers occupationally exposed to ionizing radiation experience an increased risk of hematological malignancies (Kumar et al., 2013). Ionizing radiation is a classical mutagen and is capable of inducing various kinds of stable and unstable chromosomal aberrations (Vellingiri et al., 2014). Low- and high-dose exposures to ionizing radiation result in different signaling events at the molecular level, and may involve different response mechanisms (Zhang et al., 2014; von Neubeck et al., 2015). However, different LDIR-induced responses may also share the same signal transduction pathways (Tang and Loke, 2015).

Reproductive function is sensitive to changes in the physical environment, including ionizing radiation. However, there is a paucity of data regarding the association between occupational radiation exposure and risk to human fertility (Kumar et al., 2014). Exposure to ionizing radiation leads to a high incidence of de novo mutations in the Y chromosome (Arruda, 2009). There are significant differences in the semen characteristics motility, viability, and morphological abnormality between exposed and non-exposed populations (Kumar et al., 2013).

Sperm DNA integrity is a functional parameter of male fertility evaluation (Tandara et al.,
The sperm DNA fragmentation index (DFI) is a good prognostic marker; a higher sperm DFI may be associated with a poor successful pregnancy rate, even after assisted conception, and may be associated with recurrent loss of the fetus (Venkatesh et al., 2011). Kumar et al. (2013) reported that the level of sperm DNA fragmentation was significantly higher in a group that was occupationally exposed to radiation compared with a non-exposed group. There is a paucity of new data on sperm DNA damage in men from a Chinese population who are occupationally exposed to ionizing radiation. In the present study, we report sperm quality and DNA damage in men from Jilin Province, China, who have been occupationally exposed to ionizing radiation.

MATERIAL AND METHODS

Patients

The patients were consecutively recruited among men who sought pre-pregnancy counseling in the andrology outpatient's clinic of the First Hospital of Jilin University. A total of 118 men were recommended for the detection of sperm DNA damage between January 2014 and June 2015. Simultaneously, sperm parameters were detected in all patients.

Questionnaire

Each patient was provided with a detailed questionnaire on the patients' occupation, working conditions, age, marital history, height, weight, education level, smoking history and frequency, and medical history.

Analysis of sperm parameters

Sperm concentration and motility were determined by computer-assisted semen analysis. Sperm morphology was evaluated on air-dried smears fixed and stained with Wright-Giemsa, as reported by Liu et al. (2010).

Sperm DNA integrity

Sperm DNA integrity was investigated by a sperm chromatin dispersion test using a kit for the determination of the DNA fragmentation level in spermatozoa (Boruide Biotechnology Co. Ltd., Shenzhen, China). Sperm possessing nuclei with large or medium halos were considered to have non-fragmented DNA, whereas sperm possessing nuclei with small halos or those degraded and without a halo were considered to have fragmented DNA. The halo size and dispersion patterns were determined by oil immersion bright-field light microscopy at 1000X magnification, as reported by Fernández et al. (2003) and Qiu et al. (2011). The sperm DFI = number of sperm with fragmented DNA / total number of sperm × 100. A sperm DFI < 25% is normal.

Statistical analysis

All data were analyzed using SPSS v.17.0 for Windows (SPSS, Inc., Chicago, IL, USA). Parametric variables were compared by independent sample t-tests. All results are reported as means ± SD or number (percentage). P < 0.05 was considered to be statistically significant.
RESULTS

Of the 118 subjects in this study, 46 men were occupationally exposed to ionizing radiation and 72 men were not (the control group). The occupationally exposed men were from various hospitals with diagnostic radiation facilities (mainly computed tomography). All 46 men had operated the equipment for more than two years, and were considered to have been chronically exposed to low-dose radiation, as reported by Kumar et al. (2013).

The characteristics of the men who had been exposed to ionizing radiation and those that had not are shown in Table 1. There were not statistically significant differences in age, height, weight, and smoking habits between the exposed and non-exposed men (P > 0.05), and their education level was approximately the same.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-exposed (N = 72)</th>
<th>Exposed (N = 46)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28.86 ± 3.75</td>
<td>28.26 ± 3.12</td>
<td>0.377</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>175.25 ± 3.51</td>
<td>174.78 ± 4.05</td>
<td>0.508</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>77.79 ± 3.67</td>
<td>78.13 ± 3.96</td>
<td>0.636</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cigarettes/day</td>
<td>3.76 ± 2.54</td>
<td>3.70 ± 3.04</td>
<td>0.879</td>
</tr>
<tr>
<td>Years</td>
<td>4.06 ± 2.25</td>
<td>3.50 ± 2.79</td>
<td>0.259</td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graduate</td>
<td>27 (37.5%)</td>
<td>20 (43.5%)</td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>39 (54.2%)</td>
<td>26 (56.5%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6 (8.3%)</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*P < 0.05 compared with non-exposed group.

The sperm parameters of the exposed and non-exposed men are shown in Table 2. Sperm motility and normal morphology were significantly lower in the exposed compared with the non-exposed men (P < 0.001). There were not statistically significant differences in sperm concentration between the exposed and non-exposed men (P > 0.05).

<table>
<thead>
<tr>
<th>Sperm parameters</th>
<th>Non-exposed (N = 72)</th>
<th>Exposed (N = 46)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentration (× 10^6/mL)</td>
<td>74.50 ± 13.67</td>
<td>73.84 ± 14.80</td>
<td>0.434</td>
</tr>
<tr>
<td>Motility (%)</td>
<td>25.19 ± 3.60</td>
<td>20.85 ± 3.41</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>Normal morphology (%)</td>
<td>16.72 ± 5.67</td>
<td>10.04 ± 3.63</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

*Sperm DFI was significantly higher in the exposed compared with the non-exposed men (P < 0.001; Table 3).

<table>
<thead>
<tr>
<th>Sperm parameters</th>
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<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm DFI (%)</td>
<td>14.68 ± 6.32</td>
<td>29.43 ± 4.57</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

DFI = DNA fragmentation index; *P < 0.001 compared with non-exposed group.

DISCUSSION

Chronic long-term exposure to low doses of ionizing radiation could increase chromosomal aberrations and sister chromatid exchange frequencies (Cardoso et al., 2001; Santovito et al., 2014).
Ionizing radiation exposure induces highly lethal DNA double-strand breaks in all phases of the cell cycle (Hunt et al., 2013). The occupationally exposed individuals showed higher frequencies of dicentric and acentric chromosomes compared with the normal controls (Jha and Sharma, 1991). DNA strand breaks accumulate for quite a long time after ionizing radiation exposure, indicating the development of genetic instability and an increase in carcinogenic risk for organisms exposed to a combination of harmful environmental factors (Mikhailenko and Muzalov, 2013). Sperm function is sensitive to ionizing radiation or certain environmental factors.

Sperm concentration, motility, and morphology are all useful in diagnosing male infertility (Guzick et al., 2001). Hence, we studied sperm quality and DNA damage in men from a Chinese population who were occupationally exposed to ionizing radiation. The characteristics of age, height, weight, and smoking habits did not differ significantly between those who were exposed to ionizing radiation and those who were not. Sperm motility and normal morphology were significantly lower in the exposed than in the non-exposed men. However, there was no statistically significant difference in sperm concentration. These results were consistent with the literature (Kumar et al., 2013).

Sperm DNA integrity is a functional parameter of male fertility evaluation (Tandara et al., 2014). A molecular epidemiology approach and/or the use of integrated biomarkers of sperm quality and sperm DNA damage might be useful for future research focused on the low-to-moderate dose range for diagnostic and professional exposures (Latini et al., 2012). Chater et al. (2007) reported that ionizing radiation triggers apoptosis in testicular germ cells. Kumar et al. (2013) reported that the level of sperm DNA fragmentation was significantly higher in those that were occupationally exposed to ionizing radiation. binsaleh et al. (2015) reported that Saudi male partners had increasing levels of sperm DFI (25.4), and there was a high percentage of sperm DNA damage in the male partner in infertile Saudi couples. In our study, the sperm DNA fragmentation index was significantly higher in the exposed compared with the non-exposed men. This result was consistent with the literature.

Low-dose ionizing radiation induces many late post-radiation effects by several pathways. Chronic oxidative stress is the main cause of the late post-radiation effects, including cancer, and this makes it an important adverse effect of exposure to ionizing radiation (Szumiel, 2015). Delayed mitochondrial reactive oxygen species production may cause some cell death after irradiation (Kobashigawa et al., 2015). LDIR could provide a potential mechanism, stimulate natural killer cells, and induce direct expansion and activation (Yang et al., 2014a). Borghini et al. (2015) reported evidence for a possible role of circulating cell-free DNA as a relevant biomarker of cellular damage induced by exposure to chronic low-dose radiation.

Computed tomography is a frequently used imaging modality that contributes to a ten-fold increase in radiation exposure to the public when compared with other medical imaging modalities (Kanagaraj et al., 2015). The average level of radiation experienced by a citizen of the USA in a year has doubled, mostly because of medical procedures. Computed-tomography scans are to blame for most of the rise (Abbott, 2015). Some studies reinforce the relevance of the biomonitoring of hospital workers who are chronically exposed to ionizing radiation (Santovito et al., 2014). Chromosomal damage leading to the formation of micronucleated lymphocytes is more frequent in hospital workers who are exposed to ionizing radiation (Bouraoui et al., 2013). The genotoxic effects of ionizing radiation remain for decades after exposure in subjects exposed to low-dose radiation (Sakly et al., 2013; Han et al., 2014).

**CONCLUSIONS**

In summary, chronic long-term exposure to low doses of ionizing radiation could affect...
sperm motility and normal morphology in the Chinese population. The sperm DFI was significantly higher in the men who had been occupationally exposed to ionizing radiation. Occupational exposure to ionizing radiation should be taken seriously. Sperm DNA integrity could be a functional parameter for the evaluation of occupational exposure.

Conflicts of interest

The authors declare no conflict of interest.

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REFERENCES

Sperm quality in men exposed to ionizing radiation


