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Genotoxic damage in female residents exposed to environmental air pollution in Shenyang city, China

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Abstract

Air pollution has been suggested to cause genetic damage from investigations of many biological markers that measure cytogenetic damage in humans. Here, we evaluated the genotoxic effects of ambient air pollution by investigating the extent of cytogenetic damage in human blood lymphocytes from rural and industrial female residents of Shenyang city, China, using micronuclei assays and polymorphic analyses of metabolic enzyme and DNA repair genes. After adjustment for potential confounding factors including DNA polymorphisms, industrial female residents were found to have a higher micronuclei frequency. These results provide evidence that micronuclei assays are a sensitive indicator to air pollution-induced genotoxic effects in humans.
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Keywords: Micronuclei; Lymphocytes; Polycyclic aromatic hydrocarbon; DNA polymorphism; Air pollution

1. Introduction

Epidemiological studies have suggested that long-term exposure to particulate matter air pollution is associated with increased incidence of and mortality from respiratory and lung cancers [1–3]. The annual excess of lung cancer cases due to air pollution in industrialized Western countries has been estimated to range from 30 to 150 cases per million people [4].

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Recently, it has been suggested that the mortality rates from lung cancer in China are much higher in urban areas than in rural areas [5]. Mortality from lung cancer varies substantially in different regions of China, with the highest rates generally found in the northeastern provinces [1,6]. The northeastern gradient is particularly prominent among females [6]. Shenyang city, which has the high frequency of lung cancer in China [1], is the capital of Liaoning province in northeastern China. It is an industrialized city with high air pollution attributable to multiple sources, especially coal burning for industrial purposes and residential heating. Approximately eight million tons of coals are consumed in Shenyang city each year and its air pollution level ranked second among 41 cities listed worldwide [7].

Air pollution has been suggested to cause genetic damage from investigations of a battery of biological markers that measure molecular and cytogenetic damage in human peripheral blood samples [8,9] and mutagenicity in *Salmonella* strains [10]. However, there is still a lack of epidemiological studies showing the relationships between these biomarkers and environmental pollution [11].

The micronuclei (MN) assay is one of the most sensitive markers of DNA damage, and has previously been used to investigate the genotoxicity of a variety of chemicals [12]. This MN test using interphase cells is more suitable as a cytogenetic marker than studies involving sister chromatid exchanges (SCEs) or chromosome aberrations (CAs), since it is not limited to metaphase cells and has the advantage of allowing rapid screening of large numbers of cells [13]. MN are formed from acentric chromosome- or chromatid-type fragments and whole chromosomes that have lagged behind in cell division, and are left outside both daughter nuclei. Thus, the MN assay has been used to investigate the effects of clastogens and aneuploidogens after occupational or environmental exposure in human epidemiological studies as well as in animal experiments [14–21]. Recent evidence also suggests that the MN assay can be useful for screening carriers of specific mutations that indicate cancer susceptibility [22,23].

The *CYP*1*A*1 gene encodes aryl hydrocarbon hydroxylase, which catalyzes the first step of the metabolism of polycyclic aromatic hydrocarbons (PAHs) to electrophilic compounds. The gene is induced by exposure to substances such as dioxin, B(a)P and other PAHs [24]. Glutathione *S*-transferases (GSTs) are one of the major groups of detoxifying enzymes. The gene encoding the *GSTM1* isoform is polymorphic. Variant *0 (null allele) causes a lack of enzyme activity in the homozygous form, which is associated with a reduced efficiency in binding genotoxic substrates, including epoxides derived from PAHs [25]. *GSTT1* is another polymorphic gene among the GST supergene family. Human erythrocytes express *GSTT1* and sequester the reactive conjugates formed during its 'detoxifying' activity, thereby preventing their genotoxic attack on DNA [26]. In fact, numerous epidemiological studies have indicated that these metabolic enzyme gene polymorphisms may have important roles in the induction of MN [27–29]. The *XRCC1* (X-ray repair cross-complementing group 1) is considered to be involved in the repair of DNA single-strand breaks after base excision repair of damage produced by ionizing radiation, alkylating agents, and reactive oxygen species. Several variants of *XRCC1* have been described, including one affecting codon 194 in exon 6 that results in an Arg to Trp substitution ($XRCC1^{194}$), one affecting codon 280 in exon 9 resulting in Arg to His substitution ($XRCC1^{280}$) and one affecting codon 399 in exon 10 that results in Arg to Gln substitution ($XRCC1^{399}$) [30]. The *XPD* and *XRCC3* repair genes polymorphisms as well as three *XRCC1* polymorphisms have little effect on the baseline level of MN in in vivo study [31]. Recently, in vitro study using EM9 cells indicated that $XRCC1^{399}$ influences repair abilities resulting in the differences in the MN frequencies [32].

Taking into account the advantages of assaying MN and several metabolic and DNA repair gene polymorphisms, we evaluated the genotoxic effects of air pollution on female residents in an industrial area of Shenyang city

2. Materials and methods

2.1. Subjects

The study population consisted of 129 healthy Chinese non-smoking female office workers from two districts in Shenyang city, in order to exclude any

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