



Oxidative Stress and DNA Damages Induced by Occupational Exposure to Asbestos: A Systematic Review

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Abstract

Background: Asbestos is one of the most important environmental and occupational carcinogens. Nevertheless, the mechanisms by which asbestos fiber exposure causes chronic diseases are not fully understood. We performed the first systematic review on the epidemiological evidence to examine the association between occupational exposure to asbestos and oxidative stress and DNA damage.

Methods: In this systematic review study, the PubMed and Scopus databases were searched for English-language publications. Eleven cross-sectional studies were included in the systematic review. A literature search was conducted by the main keywords including "Asbestos", "crocidolite", "chrysotile", "amphibole", "amosite", "Oxidative Stress", "DNA Damage", and "DNA injury". To evaluate the quality of studies, the "Newcastle-Ottawa Quality Assessment Scale" (NOS) was used.

Results: Overall, 1235 articles were achieved by searching in databases. Finally, by considering the inclusion, and exclusion criteria, 11 articles were conducted for this study. These studies were published between 1986 and 2020. Oxidative stress and DNA damage can occur in exposure to asbestos. Among various biomarkers, 8-OHdG is the best. The analysis of 8-oxodG in asbestos workers can help identify subjects with a higher level of genotoxic damage.

Conclusion: This systematic review suggests that oxidative stress and DNA damage are two main outputs of asbestos exposure. Therefore, oxidative stress and DNA damage biomarkers can be used for identifying subjects at higher risk of cancer. These findings support policy initiatives aimed at detecting and eliminating asbestos fiber exposure and preventing potential health hazards in occupational settings.

Keywords: Systematic review; Occupational exposure; Oxidative stress; DNA damage

Introduction

One of the significant environmental and occupational carcinogens associated with diverse cancer is asbestos (1). Asbestos is a naturally occur-

ring group of fibrous silicate minerals that has long been used in industry due to special properties such as heat and chemical resistance, water



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insolubility, tensile strength, and electrical insulation (2, 3). Asbestos is a group of six mineral fibers classified into two groups based on their structure: amphibole and serpentine (4). Crocidolite (blue asbestos), amethyst (brown or grey asbestos), anthophyllite, tremolite, and actinolite are rod-shaped fibers with a needle-like appearance in amphiboles, whereas serpentines contain chrysotile (white asbestos) are curved fibers. The most common type of asbestos is chrysotile (1, 5).

Asbestos was widely used in many industries in the nineteenth and twentieth centuries, with little control to protect workers from exposure. In the late 19th century, asbestos was used as a major component in construction and shipbuilding for fire protection and insulation, and as an anti-friction material for clutch and brake pads, density rings, and vehicle supports, as well as used in the filter structure. Furthermore, asbestos is used as an additive to asphalt concrete to improve the stability of the road surface (2, 6). As a result, a large number of industrial workers and a significant portion of the urban population were exposed to asbestos dust during the processes of asbestos mining and milling, asbestos-cement production and use, maintenance, shipbuilding, and manufacture's installation and isolation (7). According to WHO, approximately 125 million people worldwide are exposed to asbestos in the workplace. Asbestos exposure at work is responsible for approximately 233 000 deaths each year (8). Between 1970 and 2005, most Western countries prohibited the use of asbestos, except the United States, where it is only partially prohibited, and Canada, where the asbestos ban went into effect in 2018 (9, 10). However, the use and extraction of asbestos continues in developing countries, with approximately 2.2 million tons produced globally each year (11).

Asbestos fiber exposure is strongly linked to malignant mesothelioma and lung cancer (12). It also causes diseases such as pleural plaques thickening, asbestosis (pulmonary fibrosis), and effusion (13). Based on sufficient evidence for various types of cancer, the International Agency for

Research on Cancer (6) classified all types of asbestos fibers as known human carcinogens (group 1) in 2012. In addition to lung cancer and mesothelioma, there has been evidence of a link between asbestos exposure and cancers of the gastrointestinal tract and colon. Asbestos exposure increases the risk of cancers of the ovaries, larynx, throat, esophagus, and kidneys (14). Approximately 110,000 people die each year as a result of asbestos-related lung cancer, mesothelioma, and asbestosis (13).

The molecular mechanisms involved in the carcinogenic effects of asbestos are not yet fully understood. However, three major theories about asbestos pathogenesis are presented. According to the theory of oxidative stress, phagocytic cells generate a large number of free radicals due to their inability to digest fiber. Furthermore, epidemiological studies have revealed that asbestos fibers containing iron have a higher carcinogenic strength. Highly reactive oxygen species (12) such as hydroxyl radicals are catalyzed by iron on the surface of the fiber via Fenton-type reactions. They contribute to asbestos fiber carcinogenicity. According to the chromosome tangling theory, asbestos fibers reacted with chromosomes (directly or via the division spindle) and resulted in chromosomal abnormalities. The theory of absorption of carcinogenic molecules states that asbestos fibers concentrate proteins or chemicals in vivo, including cigarette smoke components (15, 16).

A few studies have revealed a link between oxidative stress, DNA damage, and asbestos exposure. The review of the literature reveals that there is no review study in this field. As a result, the aim of this study was to review the studies conducted on the effects of exposure to asbestos on changes in oxidative stress and DNA damage in order to identify biomarkers that can correctly identify people exposed to asbestos.

Methods

Study design

According to the PRISMA guidelines, this study was based on a systematic review of published literature (17).

Search strategy

A PubMed and SCOPUS search was conducted to identify English-language studies published between 1975 and 9 Nov 2021 about the relationship between occupational exposure to asbestos and oxidative stress and DNA damage. Various Mesh term combinations were used to search for studies that included Asbestos("Asbestos"[MeSH Terms] OR "Asbestos"[Title/Abstract] OR "crocidolite"[Title/Abstract] OR "chrysotile"[Title/Abstract] OR "amphibole"[Title/Abstract] OR "amosite"[Title/Abstract])) and that reported on associations oxidative stress, and DNA damage ("Oxidative Stress"[MeSH Terms] OR "Oxidative Stress"[Title/Abstract] OR "DNA Damage"[MeSH Terms] OR "DNA Damage"[Title/Abstract] OR "DNA injury"[Title/Abstract]). To find any additional studies, we used Google Scholar, cited references in included papers, and related review papers that came up in the search.

Inclusion criteria

This review included exposed and non-exposed studies that investigated the relationship between occupational asbestos exposure and oxidative stress and DNA damage.

We included in the systematic review all studies that met the following criteria:

- Study design: exposed and non-exposed studies;
- Studies which reported the role of occupational exposure to asbestos on oxidative stress and DNA damage;
- Original reports;

Moreover, the studies with the following criteria were excluded from the review process.

- Information on the studies was inaccessible or could not be extracted;
- Conference, reviews, case reports, letters, in vivo and in vitro studies;
- Exposure to asbestos was not occupational;
- Studies conducted among patients with mesothelioma, asbestosis, and lung cancer;
- The language of studies is not English;
- Abstract studies with inadequate and thesis;

Study selection

To begin, the titles and abstracts of all studies found through database searches and manual searches were screened to ensure their eligibility. Then, in the following step, eligible full-text articles were reviewed. Articles that lacked inclusion criteria were excluded using a screen form based on PECO (population, exposure, control, and outcomes). Disagreements were resolved through discussion among the reviewers. We only included the broader study in the systematic review when the same author reported two similar studies.

Data extraction

Data extraction was carried out by two independent reviewers who used a datasheet. They extracted information such as the first author, publication year, country, age range, gender, sample size, occupation, duration of exposure, investigated oxidative stress biomarkers, outcome and confounders. Discussion with the third author resolved a disagreement in data extraction.

Quality assessment

The assessment of the quality of studies included in systematic reviews is critical for the interpretation of those reviews. Because of the methodological complexities, the frequent use of data originally collected for purposes other than research, and the subjective nature of the quality evaluation, assessing the quality of observational studies is difficult. A number of tools have been provided to check the quality of these studies.

One of the best of these tools is Newcastle Ottawa. Two authors independently assessed the quality of each article included in this systematic review using the "Newcastle-Ottawa Quality Assessment Scale" (NOS)(18). Depending on the type of study, this checklist has been tailored separately for cohort, case-control, and cross-sectional studies. Due to the cross-sectional nature of all incoming studies, an adapted checklist for cross-sectional studies was used in this study. This checklist is divided into three sections. It consists of seven items: selection (four items), comparability (one item), and outcome (two items). A study can only receive one star for each numbered item in the Selection and Exposure categories. Comparability can receive a maximum of two stars. The total number of stars indicates the quality of the study. The highest quality score that an article can receive is a '9'. Studies with a score of 9 were considered high quality, while studies with a score of 7-8 were considered moderate quality. Studies with a score less than 7 were of poor quality.

Results

Study selection

A search of the EMBASE (via Scopus) and MEDLINE (via PubMed) databases in 2021 yielded 1226 studies (MEDLINE n=455; EMBASE n=771). Furthermore, a manual search of Google scholar and the reference lists of included studies and related reviews yielded 9 references. After duplicate records were removed, 866 articles remained in the title and abstract screening. Only 40 of these articles were accepted for full-text review. Following the full-text review, 29 of these articles were excluded because they did not meet the inclusion criteria. Finally, the systematic review included only 11 studies. Our study selection process is depicted in Fig. 1.

Study characteristics

As shown in Table 1, 11 studies have looked into the link between occupational asbestos exposure and oxidative stress and DNA damage. The studies included were published between 1986 and 2020. Most studies had been conducted in Europe (Germany (19, 20), Slovakia (21), Czech Republic (22), and Italy (3, 7, 23, 24)), followed by Asia (Japan (25) and Iran (15)), and North America (Canada (26)). With respect to design, all studies were cross-sectional, and their sample sizes ranged from 12 to 850 people. five studies in the general population included both genders (19-23), five studies only included males (3, 15, 24-26), and one study did not mention gender (7).

Quality assessment of reviewed studies

The quality of studies is one of the criteria that can influence the study's outcome. In an assessment based on study quality score, studies with a score of 9 were classified as high-quality studies, studies with a score of 7-8 were classified as moderate-quality studies, and studies with a score of less than 7 were classified as poor-quality studies. We discovered that the majority of studies were of poor quality (3, 7, 15, 19-23, 25, 26), with only one study being of moderate quality (24). None of the included studies was of high quality. The most serious flaw in these studies is related to the selection and comparability section. The majority of these studies did not describe the sampling strategy. Moreover, none of the information studies related to the response rate or the characteristics of respondents and non-responders is mentioned. A description of the measurement tool for ascertainment of asbestos exposure is not described in most of these studies. Furthermore, while confounding factors can influence study results, they have only been partially controlled in a small number of studies and have been explicitly mentioned in only one.

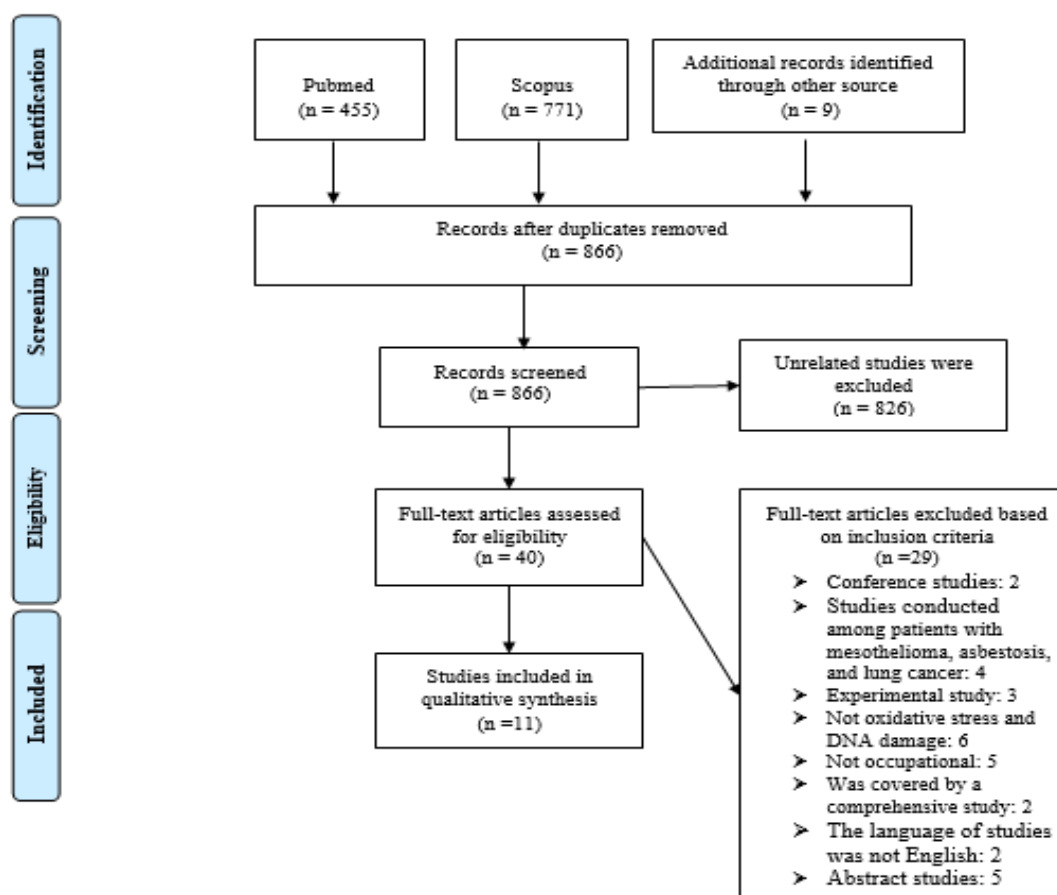


Fig. 1: Flow diagram of the screening process and study selection

Table 1: Characteristics of the included studies

First Author (year)	Location	Sample size	Gender	Occupation	Duration of exposure	Outcome	Oxidative stress biomarkers	Quality score
Kelsey K. T. (1986) (26)	Canada	12	Male	Construction trades	30.2	Asbestos exposure was not associated with increased susceptibility to BP-induced SCE or an increase in baseline SCE.	The frequencies of base-line and benzo[a]pyrene - induced sister chromatid exchanges (SCE)	3
Marczynski, B. (2000)(20)	Germany	850	Male, Female	-	<11->40	Asbestos fibers cause oxidative DNA damage in humans, which contributes to the formation of malignant tumors.	8-OHdG levels in WBC DNA	6
Marczynski, B. (2001)(19)	Germany	813	Male, Female	-	>19	Changes in LMW-DNA fragmentation were discovered in the asbestos workers studied when compared to the DNA fragmentation pattern of controls.	LMW-DNA fragmentation	6

Yoshida, R.(2001)(25)	Japanese	48	Male	Construction workers	-	The results revealed that the levels of 8-oxodG and biopyrins in the defined asbestos-exposed group were higher, Though not statistically significant, than those in the control group.	8-oxo-7, 8-dihydro-2'-deoxyguanosine (8oxodG) and biopyrins	3
Dusinská, M. (2004)(21)	Slovakia	164	Male, Female	Asbestos cement plant workers	5-40	The levels of oxidized pyrimidines were significantly higher in exposed men than in non-exposed men. Furthermore, oxidised pyrimidines and alkylated bases were found to be strongly related to years of occupational exposure. The frequency of micro-nuclei did not differ between exposed and control subjects. When compared to the control group, exposed asbestos workers had significantly more chromosomal aberrations.	DNA damage (strand breaks [SBs], base oxidation and alkylation); cytogenetic parameters; and individual DNA repair capacity (incision at 8-oxoguanine)	5
Pelclová, D. (2008)(22)	Czech Republic	138	Male, Female	Asbestos manufacturing plant workers	24.1 ± 2.0	The asbestos-exposed group had higher levels of 8-isoprostane, ESR 1.H, ESR 2.H, 1-microglobulin, and 1-antitrypsin than the control group. The presence of rheumatoid factor was more common in exposed people than in controls.	8-isoprostane	4
Marini, V. (2011)(7)	Italy	66	-	-	-	The % ages of micronucleated mononucleated lymphocytes (MnMNL) and micronucleated binucleated lymphocytes (MnBNL) differed from controls in a statistically significant way (MnBNL). The correlation between the frequency of the three types of micronucleated lymphocytes and the serum-SMRP levels of asbestos-exposed subjects was statistically significant for MnMNL but not for MnBNL or MnPNL.	Micronucleus (Mn) frequencies in peripheral blood lymphocytes (PBL)	6
Tomasetti, M. (2011)(23)	Italy	72	Male, Female	-	23.3 ± 10.7	Compared to controls, asbestos-exposed subjects showed a significant increase in the lymphocyte	8-oxodG, and DNA SSBs	5

Afaghi, A. (2015)(15)	Iran	100	Male	Asbestos cement plant workers	5	8OHdG levels. Lymphocytes of asbestos-exposed subjects showed a higher basal DNA damage (SSB-b) and were more susceptible to oxidation (nSSBs) compared to the controls. . Workers had higher blood levels of DNA damage and MDA than the control group. When compared to the control group, the workers had lower TTM. There was no discernible difference in TAC levels between the groups.	Malondialdehyde (MDA), total thiol molecule (TTM), total antioxidant capacity (TAC), and DNA damage, 8-hydroxy-2-deoxyguanosine (8-OH-dG) as an index of DNA damage	4
Bonassi, S. (2017)(3)	Italy	327	Male	Mechanical, petrochemical and marine jobs, building industries, pottery and ceramic plants.	11.5 ± 8.1	Adduct frequency was significantly higher in exposed subjects than in controls.	3-(2-deoxy-β-D-erythropentafuranosyl) pyrimido[1,2-α]purin-10(3H)-one deoxyguanosine (M1dG) adducts	6
Cellai, F. (2020)(24)	Italy	185	Male	Former exposed workers: chemistry, metal-mechanics and ship-building sectors as repairmen, equipment operators, carpenters and mechanics Current asbestos workers : construction industry and residential building settings workers	8.5 ± 6.4	The frequency of 8-oxodG per 105 deoxyguanosine was significantly higher among exposed workers than among controls. When the relationship with occupational history was investigated, it was discovered that current and former asbestos workers had significantly higher levels of 8-oxodG than healthy controls. After stratification for occupational history, workers with 10 or more years of prior asbestos exposure had a significant 194 % excess of adducts.	8-hydroxy-20-deoxyguanosine (8-oxodG), in the leukocytes	7

Occupational exposure to asbestos

The most common source of asbestos exposure is occupational exposure. There are 125 million people in the world who work in an environment where they are exposed to asbestos. Asbestos minerals were previously used as raw materials in the asbestos cement industry, building, train and ship insulation, textile products, adhesives, and friction materials (27). Workers in these manufacturing sectors were exposed to asbestos at levels likely greater than 20 f/ml in air, resulting in a cumulative asbestos dose, weighted by fiber type, that was mostly greater than 200 f/ml*years. Despite the fact that many countries have banned the use of asbestos, particularly chrysotile, is still widely used as a construction material in some parts of the world due to its low cost, durability, and thermal properties. Russia, China, Kazakhstan, and Brazil are now the leading producers of asbestos, with the majority of the material extracted being used in Asia and Eastern Europe (28, 29).

Studies included into this systematic review were conducted on workers in asbestos production (22), asbestos cement (15, 21), pottery and ceramics (3), construction and residential building settings industries (25, 26). Mechanical, petrochemical, and marine occupations (3) were also among the other jobs studied. The majority of former asbestos exposure workers had worked as repairmen, equipment operators, carpenters, and mechanics in the chemistry, metal, mechanics, and shipbuilding sectors (24). On the other hand, current asbestos workers were subjects who worked in the construction industry and residential building settings (24), which are still considered at high risk of asbestos contamination even after the bans (IARC 2012) (14). Individuals' occupations were not determined in some of these studies.

Asbestos is classified into several types, each of which has different uses depending on its properties. Only two of the reviewed studies specified the type of asbestos to which workers are exposed. Workers were primarily exposed to crocidolite asbestos. Crocidolite exposure was found

in 18.2% of workers, either alone or in combination with other types of asbestos (also chrysotile) (19, 20). Furthermore, according to the study of Pelclová et al, approximately 95% of the asbestos in the asbestos production plant is chrysotile and 5% is crocidolite (22).

Exposure assessment

Three of the studies reviewed measured occupational asbestos exposure. In two of these studies, electron scanning microscopy was used to identify asbestos fibers, analyze fiber morphology, and quantify collected samples.

Dushinska et al. investigated occupational exposure at the asbestos plant from 1956. Fiber dust concentrations ranged between 40 and 60 mg/m³ between 1956 and 1960, and 10–34 mg/m³ between 1960 and 1977. Since 1978, numerical concentrations have also been evaluated. Between 1978 and 1990, exposure levels ranged from 2–11 fiber/cm³. These concentrations fell over time, and from 1991 to 1994, exposure ranged between 1 and 4 fiber/cm³. Between 1995 and 1998, the exposure ranged between 0.4 and 1 fiber/cm³. Asbestos levels in the production hall were 3–5 times higher than the Slovak occupational limit (0.001 fiber/cm³ for indoor areas where asbestos was used as a building material). The administrative area of the factory had levels that were lower than this limit (21).

Asbestos exposure classified into four categories (Fibers 15 (Class 4F), Fibers 15–25 (Class 3F), Fibers >25–50 (Class 2F), and Fibers >50 (Class 1F)) based on a quantitative approach described by the Hauptverband der gewerblichen Berufsgenossenschaften in Germany and adopted by INAIL in Italy. This quantitative approach calculates the "fibers-day" concentration (C) using the formula $C = Ftk$, which takes into account both the concentration of asbestos fibers in the specific working environment (F) and the eight hours of exposure per day (t), multiplied by a constant ($k = 5.21104$), which represents the total number of working hours over a year (7).

Because no direct data on f/mL years or asbestos type were available in the other included studies,

the intensity of exposure was estimated based on exposure duration. In these studies, the duration of asbestos exposure was at least five years. In some of these studies, workers with a history of exposure to 40 years or more have been studied. In these studies, exposure assessment was conducted using filling out the questionnaire and doing the interview.

Biomarkers

Oxidative stress is defined as an imbalance in the body's free radicals and antioxidants (30). The body's cells produce free radicals such as ROS during normal metabolic processes, which are generally balanced by antioxidants (31). To assess ROS, a variety of markers has been examined at the cell or biological sample level (30). These biomarkers include 8-hydroxy-2'-deoxyguanosine (8-OHdG), isoprostane (IsoPs), malondialdehyde (MDA), S-glutathionylation, Oxidised low-density lipoprotein (OxLDL), myeloperoxidase (MPO), and others (32). In this systematic review, various biomarkers were examined in reviewed studies to evaluate the oxidative stress and DNA damage effects induced by occupational exposure to asbestos fibers. 8-OHdG levels have been studied as one of the main markers of oxidative stress and DNA damage in most of the reviewed studies. In addition, the frequencies of sister chromatid exchanges (SCE), low molecular weight (LMW) fragmented DNA, DNA SSBs, bioperine, strand breaks [SBs], base oxidation and alkylation, Malondialdehyde (MDA), total thiol molecule (TTM), and total antioxidant capacity (TAC) were assessed as indicators of oxidative stress and DNA damage.

8-isoprostane is another oxidative stress biomarker studied by Pelclová et al. According to this study; the asbestos-exposed group had higher levels of 8-isoprostane than the control group (22).

The Afaghi et al study also looked at MPA, TTM, and TCA. Workers exposed to asbestos had higher blood levels of MDA than the control group. In contrast, TTM rates were lower among exposed workers than among non-exposed

workers, and no discernible difference in TAC levels existed between the groups (15).

The levels of oxidized pyrimidines in exposed men were significantly higher than in non-exposed men. In addition, alkylated bases and oxidized pyrimidines were strongly associated with years of occupational exposure (21).

Kelsey et al demonstrated in 1986 that asbestos exposure did not increase susceptibility to SCE or baseline SCE. However, the results of this study may be far from accurate due to the low quality of the study (26).

In addition to oxidative stress, some studies have examined the effect of occupational exposure to asbestos on DNA damage, which shows that blood levels of DNA damage are higher in workers who have been exposed to asbestos.

Marczynski et al. found changes in the fragmentation of LMW-DNA in asbestos-exposure workers compared with the pattern of DNA fragmentation in the nonasbestos-exposure group (19).

The frequency of micronuclei did not differ between asbestos workers and control. In contrast, workers exposed to asbestos had significantly more chromosomal aberrations (21).

The % ages of micronucleated binucleated lymphocytes (MnBNL) and micronucleated mononucleated lymphocytes (MnMNL) of asbestos-exposed workers were statistically different from control groups. The frequency of the three types of micronucleated lymphocytes and the serum-SMRP levels of asbestos-exposed subjects correlated statistically for MnMNL but not for MnPNL or MnBNL (7).

Furthermore, lymphocytes from asbestos-exposed subjects had higher basal DNA damage (SSB-b) and were more susceptible to oxidation (nSSBs) than controls (23). Moreover, workers had higher blood levels of DNA damage than the control group (15).

Discussion

Despite the 1976 ban on the extraction, manufacture, and processing of asbestos products (Di-

rective 2003/18/EC); and the subsequent 2005 ban, chronic asbestos-related diseases continue to be a common clinical problem and an important health concern worldwide. Nevertheless, the mechanisms by which asbestos fiber exposure causes chronic diseases are not fully understood (6, 14). Therefore, it is valuable to study the relationship between exposure to asbestos and the blood and urinary levels of biomarkers of oxidative stress and DNA damage, especially in workplace environments. Indeed, biomarkers, such as Oxidative stress biomarkers, can be used to assess the genotoxic effects of carcinogens in different occupational settings (33, 34). Thus, by identifying appropriate biomarkers, the risk of chronic diseases such as cancer among asbestos-exposed workers can be predicted and prevented from progressing. Therefore, we performed the first systematic review to investigate the association between occupational exposure to asbestos and the risk of oxidative stress and DNA damage in observational studies. Thus, we tried to find the best biomarker to use in assessing the risk of asbestos exposure.

According to the results of this review, significant changes in the biomarkers of oxidative stress and DNA damage were observed in biological samples of asbestos-exposed workers, supporting the hypothesis of oxidative stress and DNA damage for the destructive effects of asbestos fibers. Our investigation shows that past occupational asbestos exposure appears to be a relevant source of genetic damage in both current and former workers' blood. The biomarkers of oxidative stress are diverse, as shown in Table 1. However, 8-oxodG has received the most attention, and in all cases that occupational asbestos fiber exposure results in the formation of large amounts of 8-oxodG (15, 20, 23-25, 35). Asbestos workers have high levels of 8-oxodG after being exposed to occupational asbestos fibers.

These findings are significant because high levels of 8-oxo-dG increase the likelihood of mutagenic G: T-transversions during cell division, which are frequently found in tumor-related genes. These findings support the use of such compounds in

worker leukocytes to detect high-risk individuals in a group of workers. Furthermore, the 8-oxodG can be used for reliable biological monitoring of workers with prior asbestos fiber exposure (24).

The mechanisms underlying the production of 8-oxodG by this carcinogen (asbestos) in workers may be due to fiber accumulation on the pleural surface and interaction with the mesothelial cell layer, which can result in the formation of free radicals. Chronic inflammation caused by macrophages' prolonged phagocytic activity while destroying persistent fibers can result in high ROS levels (25). The existence of catalytic iron on the surface of asbestos fibers can also be a chief source of ROS. As the level of iron on the asbestos surface increases, its mutagenicity also increases. Amphiboles, for example, have a higher iron concentration than serpentines, which are more mutagenic. This variation in iron level in harm potential could be attributed to variations in the activity of the surface iron. Fenton-type reactions catalyzed by iron on the asbestos fibers can generate free radicals (36), which diffuse to peripheral blood cells via the lung microvascular endothelium (37). ROS produced by persistent inflammation and the activation of neutrophils and macrophages in the lung parenchyma can indirectly cause 8-oxodG (14). Several mechanisms have been identified by which chrysotile asbestos fibers cause pulmonary disease (38); however, inflammatory cytokines and ROS caused by the pleural accumulation of asbestos fiber exposures appear to be associated with various types of DNA damage, which can induce oncogene activation, cell proliferation, and increased susceptibility to mutations.

Chronic asbestos-related diseases can have a long latency period; for example, the incubation period for lung cancer is 10-20 years, and for malignant pleural mesothelioma 50 years (14). This study showed that past occupational exposure to asbestos could be a source of genetic damage in workers. An increase in 8-oxodG was observed in workers who had been employed in asbestos-related occupations for a long time. The for-

mation of oxidative adducts may reflect the concentrations of asbestos fibers in the lung parenchyma. Therefore the burden of persistent asbestos fibers in the lung appears to play an important role in increasing the levels of 8-oxodG in former asbestos workers.

However, the study populations worked in a variety of environments, including the mechanical, petrochemical, marine, and construction industries, as well as ceramics and pottery factories. Therefore, workers could have been exposed to other volatile carcinogens at the same time. Therefore, high levels of 8-oxodG may indicate concurrent exposure to other volatile carcinogens in the workplace, such as formaldehyde, silica dust, heavy metals, polycyclic aromatic hydrocarbons, and aromatic amines.

There are some limitations to this systematic review; first, the number of studies that met the inclusion criteria was small. Second, the quality of the studies was relatively low. Third, no homogeneous studies were available for meta-analysis. Fourth, we could not check out different types of asbestos due to inadequate information. Finally, dose-response analysis was not practicable to determine the effect of the severity of asbestos exposure on the amount of biomarker generated. Therefore, the relationship between the concentration of asbestos that the worker encounters and the amount of biomarker created in the body was not clear. As a result, additional research is advised.

Conclusion

This systematic review has been conducted on the effects of occupational asbestos exposure on changes in oxidative stress and DNA damage. Oxidative stress and DNA damage can occur in exposure to asbestos. To evaluate the oxidative stress induced by asbestos, a variety of biomarkers such as 8-OHdG, IsoPs, MDA, S-glutathionylation, OxLDL, MPO, etc are tested. Among these biomarkers, 8-OHdG is the best. The analysis of 8-oxodG in asbestos workers can help identify subjects with a higher level of geno-

toxic damage, which implies a higher risk of lung cancer and other chronic diseases. This method can be used for medical surveillance programs of workers who have previously been exposed to asbestos, as well as for identifying subjects at higher risk of cancer. In this case, biomarkers can identify subgroups at higher risk, necessitating more intensive clinical surveillance, or they can be studied further for possible individual risk assessment. Our findings support policy initiatives aimed at detecting and eliminating asbestos fiber exposure, as we investigate potential health hazards in occupational settings.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

Conflict of interest

The authors declare that there is no conflict of interests.

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