REVIEW

An Overview of Asbestos and Malignant Pleural Mesothelioma: An Iranian Perspective

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Abstract

Asbestos refers to a group of minerals that appears naturally in the environment as bundles of fibers. The incidence rate of asbestos-related diseases has considerably increased as well as the amount of asbestos utilization in few countries. Malignant pleural mesothelioma (MPM) is a rare type of aggressive and life threatening neoplasm which arise from various serous surfaces: pleura, peritoneum, tunica vaginalis and pericardium. The first case of MPM was reported in 1947. MPM etiologically is associated to the exposure of asbestos fibers. This form of malignancy is difficult to diagnose in paraclinical work-ups because mesothelioma could occur within 10-20 years of the first-time exposure to asbestos. The burden of MPM is not yet to be wholly understood. The toxic side effects of asbestos on environment and people compelled the European countries to accept the French view upon this matter. However, this approach has not been accepted by some developing countries. This review provides a brief points and facts in relation to MPM and asbestos in Iran.

Keywords: Mesothelioma- pleura- asbestos

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Introduction

Malignant pleural mesothelioma (MPM) is a rare type of aggressive and life threatening neoplasm in most cases (Pérez-Guzmán et al., 2016). The tumor is etiologically associated to the exposure of asbestos fibers in almost 80% of cases (McDonald et al., 1996). This form of malignancy is difficult to diagnose in paraclinical work-ups. The median survival period of malignant pleural mesothelioma, 9 to 12 months, describes the low rate of life expectancy among patients suffering by this disease (Taioli et al., 2015). Since the 1950s reported incidence of MPM has gradually increased in industrial countries (Robinson., 2012). There are several histologic subtypes of malignant mesotheliomas which are classified according of their morphologic and immunohistochemical features (Kakiuchi et al., 2016). Main types of malignant mesotheliomas are epithelioid, sarcomatoid, and mixed (biphasic).

As a fatal type of malignancies, mesotheliomas arise from various serous surfaces: pleura (65-70%), peritoneum (30%), tunica vaginalis testis (0.3% to 5%), and pericardium (1-2%) (Mak et al., 2004; Bridda et al., 2007). MPM is responsible for one percent of all types of cancers. As a consequence of occupational factors, the disease is mostly common in males than it is in females (Price et al., 2004). Malignant mesothelioma could occur within 10- 20 years of the first-time exposure to asbestos (Moore et al., 2008). Although the average age of patients who die of MPM is 50-70 years in two third of cases, it could be life threatening at any age (McElvenny et al., 2005). MPM happens in White and Spanish individuals much more than in African, American, and Asian races (Robinson et al., 2005). The burden of MPM is yet to be wholly understood. As reported by Driscoll and colleagues, 43000 deaths caused by MPM are recorded every year (Driscoll et al., 2005). Furthermore, ninety thousands out of 125 million individuals who exposed to asbestos die every year (Hodgson et al., 2005). Since exposure to asbestos usually occurs at work place, Malignant Pleural Mesothelioma is categorized in the occupational disease group) (Anna et al., 2016).

It is worth mentioning that 50% of all neoplasms which are mainly caused by occupational pathogens are related to the exposure of asbestos fibers (Department of Health Mesothelioma Service Framework., 2007).

Background

In 1933, Roodhouse Gloyne described the association between exposure to asbestos and pulmonary disorders which he called "pulmonary asbestosis" (Gloyne, 1933). The first case of MPM was reported in 1947 (Mowé et al., 1991). In 1960, the link between asbestos fibers and MPM was documented. There had been reported several cases of

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the disease in asbestos mines' workers (Musk et al.,1989). The utilization of asbestos as an insulator substance that mostly used in ship making and construction industries increased in the United States and Europe for a period of forty years, between 1940 and 1979 (Spirtas et al., 1986). Consequently, the incidence rate of this malignancy went up during the same era. However, because of the lag between exposure to asbestos and clinical diagnosis of mesothelioma, the incidence rate of the disease could not be precisely estimated in short term (Carbone et al., 2002). As far as epidemiology is concerned, the prevalence rate of this tumor mainly depends on occupational factors. In 2003, Larson and colleagues estimated that in the next 20 years, seventy thousand new cases of MPM will be found in the US (Larson et al., 2007). Furthermore, it would be expected to see 25000 new cases of MPM in the European countries between 2015 and 2020 (McElvenny et al., 2005). A recent study run in the UK shows that the highest death-rate of MPM in the world belongs to the British people who born before 1960, and diagnosed as having the disease before 1980; when asbestos usage was banned (Department of Health Mesothelioma Service Framework; 2007). Since then, the number of MPM cases decreased vigorously. This fact exemplifies the direct link between asbestos exposure and increased chance of mesothelioma incidence. Finally, according to the estimations of a British advisory group, the perspective gets worse in the next fifty years when 65,000 patients with MPM die around the world (Panou et al., 2015). Other risk factors of mesothelioma are as follow: exposure to Thorium dioxide in medical radiotherapy (Creaney et al., 2015; Faig et al., 2015), age, gender (Ohar et al., 2016), genetics (Thanh et al., 2016), and Simian Virus 40 Mohammad-Taheri et al., 2013). However, the latter is still under controversy increased in the United States and Europe for a period of forty years, between 1940 and 1979 (Spirtas et al., 1986). Consequently, the incidence rate of this malignancy went up during the same era. However, because of the lag between exposure to asbestos and clinical diagnosis of mesothelioma, the incidence rate of the disease could not be precisely estimated in short term (Carbone et al., 2002). As far as epidemiology is concerned, the prevalence rate of this tumor mainly depends on occupational factors. In 2003, Larson and colleagues estimated that in the next 20 years, seventy thousand new cases of MPM will be found in the US (Larson et al., 2007). Furthermore, it would be expected to see 25000 new cases of MPM in the European countries between 2015 and 2020 (McElvenny et al., 2005). A recent study run in the UK shows that the highest death-rate of MPM in the world belongs to the British people who born before 1960, and diagnosed as having the disease before 1980; when asbestos usage was banned (Department of Health Mesothelioma Service Framework; 2007). Since then, the number of MPM cases decreased vigorously. This fact exemplifies the direct link between asbestos exposure and increased chance of mesothelioma incidence. Finally, according to the estimations of a British advisory group, the perspective gets worse in the next fifty years when 65,000 patients with MPM die around the world (Panou et al., 2015). Other risk factors of mesothelioma are as follow: exposure to Thorium dioxide in medical radiotherapy (Creaney et al., 2015; Faig et al., 2015), age, gender (Ohar et al., 2016), genetics (Thanh et al., 2016), and Simian Virus 40 Mohammad-Taheri et al., 2013). However, the latter is still under controversy. The following countries are responsible for 90% of asbestos production in the world: Russia, China, Brazil, and Kazakhstan. Canada, which belonged to this list some years ago, has changed its strategic plan upon this in order to strictly control asbestos usage.

Asbestos and Mesothelioma in Iran

The first time appearance of asbestos in Iran backs to the early twenties century. In 1908, a German company named "Iraniat" started the production of asbestos cement by the same name. Prior to the World War II, the substance used by the German engineers were constructing the Iranian railway networks. The only asbestos mine in Iran is located in the eastern area of the country. It was established in 1974 and was shut down in 2003. The mine was producing 3000 tons of asbestos each year (Kakooei et al., 2010). Because of the low price of asbestos and its wide field of usage, Iran has become one of the main importers of the substance. Nowadays, asbestos is still in use in more than 50 industrial establishments across the country with an approximate of 5,000 employees. It is used in manufacturing cement layers, as well as pipes, tiles, kilns, warm tubes, sheets clothes, and so on. The annual usage of asbestos in Iran has jumped from 10,000 tons to 100,000 tons with 90% in cement based productions and 10% in car-making factories. As an example, a car-making company with 3,000 personnel is using 20,000 tons of asbestos each year. Unfortunately, the amount of asbestos exposure in these factories is much higher than the standard global ratio. As reported by Kakooei and colleagues, the concentration of chrysotile fibers in these companies are 8 times higher than Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) (Kakooei et al., 2009).

However, the problem does not stop here. The fact that Tehran has been built on hillside causes more pollution; drivers need to apply brakes and clutches more frequently than usual. The distribution of asbestos fibers is directly related to the number of vehicles passing across an area. It was stated that maximum amount of asbestos concentration in non-occupational environment was detected in central and northern areas of Tehran. In 2010, the maximum and minimum levels of asbestos fibers in the air were 0.1 and 0.0057 fiber/ml, respectively (Kakooei et al., 2013). Using Scanning Electron Microscopy (SEM), Kakooei and colleagues (Kakooei et al., 2013) measured the concentration of asbestos fibers in 110 outdoor places of Tehran. Their findings showed that the average amount of asbestos concentration was 1.6×10^{-2} SEM f ml−1. The figures were much higher than most of the European countries (i.e., Italy: 5.6×10^{-4} SEM f ml^{-1}). The fibers get inhaled by the passer byes and entre to their respiratory system. The authors of the study believed that by continuous breathing for 8 hours in central areas of Tehran, approximately 8,000 asbestos fibers go through the respiratory system. The teratogenic effects of asbestos on human wellbeing convinced the

investigators of the study to claim that the level of asbestos fibers in the air must be decreased to zero (Kakooei et al., 2014). To reach this goal, firstly, asbestos usage must be banned in all industrial fields. Secondly, the current concentration of the fibers must be kept at the minimum level. Furthermore, investigations show that asbestos concentration in clutch/brake repair centers is much higher than the OSHA permissible limit (Kakooei et al., 2014). Similar results apply to areas of Tehran in which old buildings get deconstructed (Pouryaghoub et al., 2014). These findings reapprove the association of asbestos exposure and mesotheliomal malignancies. According to Pouryaghoub and colleagues claim, 53% of patients with mesothelioma had positive history of occupational exposure to asbestos (Pouryaghoub et al., 2014). Taking mesothelioma into account, the abovementioned facts emphasize the important role of prevention; the malignancy is still incurable.

A national recording system that covers 80 to 90 percent of all cancer types has documented 5 cases of mesothelioma in 2005. The number of reported malignant mesothelioma went up in 2008 when 65 cases were found. According to the database of Ministry of Health, 76 patients with malignant mesothelioma were detected in 2009. On a smaller scale, based on the archive of Masih Daneshvari Hospital (National Research Institute of TB and Lung Diseases, Tehran, Iran), a referral centre for lung diseases, 60 patients with MPM admitted between 2010 and 2013 (Najmi et al., 2014). In 2010, the Thoracic Cancer Registry Centre of the hospital was established. Since then, 1400 cases of thoracic cancers, including 110 cases of MPM, have been registered Approaching the problem of asbestos-related diseases

a. Internationally

The incidence rate of asbestos-related diseases has considerably increased as well as the amount of asbestos utilization in few countries. This fact drew attentions in the 13th session of the International Labor Organization (ILO) in collaboration with the World Health Organization (WHO) (WHO, 2007). The two bodies strongly stressed that all countries may need to think deeper on the issue of handling asbestos victims in the future. The both organizations disclosed documents showing that the Crysotile asbestos was still widely used by most countries around the world. In order to deal with the next wave of asbestos-related diseases, they proposed that members should prepare themselves by developing a national plan/guideline aimed to eradicate asbestos-related mesothelioma. Their program encourages all countries to: develop a national profile of asbestos, define their strategic policies, set up periodical notifications, and specify their fundamental strategy towards the elimination of the diseases. The two organizations support their members by making plans and consultations, collecting and sharing the information of a safer substance as the replacement of asbestos, and introducing new methods of managing the asbestos-related diseases. During the 16th annual session of the WHO and ILO in 2007, all the members declared that a global conflict program must be employed to eliminate the irreversible asbestos- related diseases. To achieve the goals of the program, all members agreed to follow the strategic policies and the fundamental activities in abolishment of the asbestos- related diseases. The national program of elimination the asbestos-related diseases (NPEAD) has been accepted as the referral policy by all members of the WHO.

Policy defines the presence of asbestos-related diseases based on its significant manifestations, and provides the crucial key strategies to face those (Salehpour et al., 2010). The first priority of the NPEAD in protection of labors is to eradicate the asbestos-related diseases. Hence, governments not only ought to accomplish the program legitimately, but to follow and fulfill the NPEAD requirements. The NPEAD determines the strategic objectives as well as the mechanisms of development, interposing and evaluating, guiding, specifying the role of each ministry. Finally, the in charged institutions should be convinced to prepare their progress report on a routine basis. The two critical parts of the NPEAD say:

1. It is necessary to estimate the amount of asbestos consumption. The estimation can be easily done by approximating the number of individuals who are currently considered as high risk in developing asbestos-related diseases. Moreover, the program would provide information needed in estimating the number of people who suffered by the asbestos-related diseases in the past.

2. The estimated numbers should be evaluated by a series of technical tools that enable us to practically assess the accessibility of the NPEAD purposes, based on their importance. The executors' performance should be continuously monitored to see whether the progress has met the program's requirements. The key characteristics of the plan are its adequacy in evaluation of the performers, and also the situational compatibility it provides for each country. Supervision of the executors' progress must be assigned to an expert team. The team is allowed to command the executors and make orders if necessary. The team is also responsible for management and evaluation of the NPEAD regulations. The team includes representatives of the following ministries: Health, Mines, Labor, Finance, and Natural Resources (Salehpour et al., 2010).

b. Nationally

Iran joined the Rotterdam Convention in1993, and became a member of the institution. The convention obliges members to undertake essential safety measures for certain perilous chemotoxic materials. In 2000, the Iranian government officially ordered the factory owners to stop using asbestos in their products. Furthermore, in September 2012, importation of white asbestos was absolutely banned by the government. The Ministry of Mines and Commerce was compelled to replace it with a safe material.

In conclusion, as a matter of fact, there are still discrepancies between what is said in official reports, and what is happening in the real world. Consequently, decision makers and supervisors are not facing a clear perspective. This article tries to elucidate the scene, and to remind policymakers of the long term troubles of asbestos usage. The authors believe that it is possible to provide a national asbestos atlas by measuring the concentration

of asbestos fibers across the country and applying the results to the GPS technology. Moreover, we will be able to design a predictor model which foresees the incidence rate of malignant mesothelioma for the next 10 years. It is worth mentioning that the aim of all these efforts is to help decision makers in elimination of asbestos-related diseases. The authors also suggest that the Canadian approach to the issue could be considered as a road map for countries such as Iran, which are still challenging with the problem of asbestos.

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