Internal Medicine and Medical Investigation Journal
E-ISSN: 2474-7750
Homepage: www.imminv.com

ORIGINAL ARTICLE

Mustard Gas Effects on Iranian Veterans After 20 Years as Shown on Chest High-resolution Computed Tomography: A Follow-up Study

Seid Kazem Razavi Ratki[1], Nasim Namiranian[2], Abdu-Reza Sadrarhami[1], Ali Ahmadi Dahaj[1], Mohammad Sobhan Ardakani[1], Reza Nafisi Moghadam[1]*

[1]*Department of Radiology, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*

[2]*Yazd Diabetes Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*

Corresponding Author: Reza Nafisi Moghadam, E-mail: moghadam@ssu.ac.ir

ARTICLE INFO

Article history
Received: Jan 17, 2018
Accepted: April 28, 2018
Published: Sep 15, 2018
Volume: 3
Issue: 3

Conflicts of interest: None
Funding: None

Key words
Chemical Weapons,
Mustard Gas,
Iran,
Veterans

ABSTRACT

Introduction: Mustard gas is a known chemical weapon that was used in the 1980-1988 Iran-Iraq War. It causes many health problems, including serious respiratory damage. In this study, we used high-resolution computed tomography to assess the pulmonary complications after 20 years of veterans of the Iran-Iraq War who were exposed to mustard gas. **Materials and Methods:** This was a follow-up study conducted on 200 Iranian veterans with a history of exposure to mustard gas at least 20 years previously. High-resolution computed tomography was performed on all veterans and was interpreted by two independent expert radiologists who were blinded to the study. The frequency of high-resolution computed tomography findings was reported. Data were analyzed with statistical package for the social sciences version 20 software. **Results:** One hundred twenty veterans (60%) showed HRCT abnormalities. The most frequent high-resolution computed tomography findings were diffuse hyper-aeration, 63 (52.5%); interstitial opacity, 50 (41.7%); parenchymal opacity, 26 (21.7%); bronchiectasis, 15 (12.5%); sub-pleural air trapping, 13 (10.8%); and local fibrosis, 10 (8.3%). Generally, lower lobes were more frequently affected. **Conclusion:** This study showed a high frequency of abnormal high-resolution computed tomography findings in veterans who were exposed to mustard gas, and most abnormalities were irreversible. These findings included diffuse hyper-aeration, interstitial opacity, parenchymal opacity, bronchiectasis, sub-pleural air trapping, and local fibrosis.

INTRODUCTION

Some chemicals, which can have significant health and environmental effects, are used as warfare agents. One of the chemicals frequently used as a chemical weapon is mustard gas. Mustard gas was first used in World War I (1). In this war, mortality due to mustard gas was 2.5% (2). The most recent use of this chemical weapon was in the 1980-1988 Iran-Iraq War (3). Approximately 10 years later, Khateri et al. evaluated survivors and found that they were suffering from respiratory (42.5%), ophthalmic (39.3%), and cutaneous (24.5%) complications (4). Mustard gas, or bis (2-chloroethyl) sulfide, is an alkylating agent with low solubility in water and high solubility in fat (5, 6). In its pure form, it is a colorless and odorless liquid, but it may have a garlicky odor due to impurities (7). This substance can readily penetrate clothing and skin and can be absorbed through the skin or respiratory tract. In its penetration pathway, it damages tissues and is then absorbed into the bloodstream. In the lungs, mustard gas can cause early and late complications (5). Early and acute effects include epithelial necrosis, accumulation of secretions and atelectasis, bronchial obstruction, hypoventilation, and hemorrhage (8). Chronic effects include chronic bronchitis, fibrosis, asthma, and bronchiectasis. Fibrosis may appear several years after exposure and can be evaluated by spirometry, diffusion capacity, and high-resolution computed tomography (HRCT) (9). It has also been shown that the incidence of lung cancer is higher in people exposed to mustard gas than the general population (10). HRCT is a powerful tool for the diagnosis of parenchymal and airway abnormalities (11).

Studies have reported varying results regarding the pulmonary complications of exposure to mustard gas. Ghanei et al. used HRCT to evaluate people with a history of exposure to various gases, and the most frequent abnormality was air trapping (38%) (12). Bagheri et al. examined 50 people with a history of exposure to mustard gas. HRCT was abnormal in all patients, and the most frequent finding was bronchial wall thickening, which was observed in all patients (13). Ghanei et al. also reported that bronchial

Published by Mehrabani Publishing LLC.

http://dx.doi.org/10.24200/imminv.xxxxxx

wall thickening was the most frequent finding, which was observed in 90% of mustard gas-exposed veterans. They found that air trapping (76%) and bronchiectasis (74%) were the next most frequent findings (14). However, Emad et al. reported that chronic bronchitis (58.8%) was the most common finding in mustard-exposed people and that bronchiectasis was not so common (15).

In our study, we used high-resolution computed tomography (HRCT) to assess the pulmonary complications after 20 years of veterans of the Iran-Iraq War who were exposed to mustard gas.

MATERIALS AND METHODS

Patients

In this follow-up study, 200 Iranian veterans with a documented history of exposure to mustard gas in the Iran-Iraq War and who showed acute or chronic respiratory symptoms were selected as study patients. The patients were consecutively selected from 500 veterans with the abovementioned conditions who were registered in a mustard gas exposure data bank.

The following data were collected: age, history of pre-exposure respiratory illnesses, smoking history, current respiratory status, and symptoms at the time of exposure. Required data were obtained from the medical files available at the main university hospital in Yazd, Iran. All patients who were smokers, who had a history of respiratory disease before exposure to mustard gas, and who had a history of occupational exposure to respiratory contaminants were excluded from the study. All selected patients did not report any pulmonary problems prior to exposure to mustard gas. Most (76%) were between 15 and 20 years of age at the time of exposure.

HRCT

Patients completed a checklist of demographic data and respiratory symptoms, after which HRCT was performed using one scanner for all selected patients (device: Shimadzu spiral CT scanner, model SCT-7800TX, Japan). HRCT images of 1-mm slice thickness were obtained at 20-mm intervals. The images were taken in both deep inspiration and deep expiration in the supine position. The non-contrast images were obtained with a window special for lung parenchyma (-100 to -200), with a width of 1600-1800.

Images were interpreted by two independent expert radiologists who were blinded to the study. Agreement was calculated by the kappa statistic. In cases of disagreement, a third radiologist interpreted the findings. A form containing demographic and radiologic information was designed for data collection. The first part included demographic data; the second part included data about HRCT. The lungs were divided into five segments: left upper, left lower, right upper, right middle, and right lower. Six findings were considered most important: diffuse hyper-aeration, interstitial opacity, lung parenchymal opacity, bronchiectasis, local fibrosis, and sub-pleural air trapping.

Data were analyzed with statistical package for the social sciences (SPSS) version 20 software. The sample size was calculated by estimating prevalence in a population considering a type 1 error of 0.05, prevalence of 0.5, and 0.06 accepted absolute differences. The findings were reported as mean ± standard deviation. The range was reported. Also, the chi square test was used. *P* values less than 0.05 were considered statistically significant.

RESULTS

All patients were men, with a mean (± standard deviation) age of 38 (± 6.2) years (range: 32-78 years). They were exposed to mustard gas about 20 years before (18.9 ± 1.3) during the Iran-Iraq War (1980-1988). HRCT examinations were obtained between January 2006 and February 2007 for each patient. All had respiratory complaints of varying intensity, including chronic cough, dyspnea, suffocation, and hemoptysis. In 80 patients (40%), HRCT was normal. The other 120 patients (60%) had various HRCT findings. Table 1 shows the frequency of HRCT findings in the patients. Diffuse hyper-aeration was the most frequent finding, in 63 (52.5%) patients, followed by interstitial opacity (41.7%), parenchymal opacity (21.7%), bronchiectasis (12.5%), sub-pleural air trapping (10.8%), and local fibrosis (8.3%).

Regardless of the type of lesion, the lower lobes in both lungs were more frequently affected than the upper lobes: on HRCT, 17 (14.2%) patients had abnormalities in the left lower lobe, 17 (14.2%) patients had abnormalities in the right lower lobe, 3 (2.5%) patients had abnormalities in the left upper lobe, and 4 (3.3%) patients had abnormalities in the right upper lobe. In 30 (25%) patients, all fields of both lungs were affected. Also, 30 (25%) patients had HRCT findings in both left upper lobe and right lower lobe segments. Table 2 shows the frequency of HRCT findings regarding the various lung segments.

The patients were divided into three groups by age. The frequency of abnormalities was compared in different age ranges, but the difference between groups was not statistically significant ($P = 0.9$) (Table 3).

DISCUSSION

Mustard gas can have deleterious effects on the human body, among the most serious being respiratory effects. In the current study, 200 Iranian veterans with respiratory symptoms who were exposed to mustard gas during the Iran-Iraq War

Table 1. Frequency of HRCT findings in Iranian veterans who were exposed to mustard gas

HRCT finding	Frequency (%)
Diffuse hyperaeration	63 (52.5)
Sub-pleural air trapping	13 (10.8)
Interstitial opacity	50 (41.7)
Local fibrosis	10 (8.3)
Bronchiectasis	15 (12.5)
Parenchymal opacity	26 (21.7)

(HRCT: high-resolution computed tomography)

Table 2. Frequency of HRCT findings regarding the lung segments of Iranian veterans who were exposed to mustard gas

Lung segment	Number (%)
Left upper lobe	3 (2.5)
Left lower lobe	17 (14.2)
Right upper lobe	4 (3.3)
Right middle lobe	6 (5)
Right lower lobe	17 (14.2)
Left upper lobe+right lower lobe	30 (25)
Left upper lobe+right middle and lower lobes	7 (5.8)
Right middle and lower lobes	6 (5)
Right and left lungs	30 (25)

Table 3. Frequency of HRCT abnormalities in different age groups of Iranian veterans who were exposed to mustard gas

HRCT findings	Age group (years)		
	30-40	40-50	>50
Normal	61 (30.5%)	16 (8%)	3 (1.5%)
Abnormal	91 (45.5%)	24 (12%)	5 (2.5%)
Total	152 (76%)	40 (20)	8 (4%)

(HRCT: high-resolution computed tomography)

were assessed radiographically. We tried to omit other predisposing factors that may cause HRCT abnormalities, such as smoking and occupational exposures. In the patients who entered the study, we did not identify any other predisposing factors, such as infections, collagen vascular diseases, and cystic fibrosis. Patients were selected from veterans who were documented to be in the Iranian town of Shalamcheh (the site of large mustard gas attacks) during the war. The study population was young (mean age: 38 years); in most other studies in Iran, the mean age is similar.

In this study, we used HRCT to assess pulmonary abnormalities, because it can more accurately delineate lung anatomy and small airways than chest X-ray and conventional CT (3, 16). Also, in the follow-up of patients with interstitial lung diseases, HRCT is a standard method (17). In the current study, 60% of patients had radiographic abnormalities, which was consistent with the study of Ghanei et al. in which 62.8% of patients had HRCT abnormalities. In our study, diffuse hyper-aeration was the most frequent finding, which was consistent with other studies (13, 15). We found that interstitial opacity and sub-pleural thickening were frequent as well. Interstitial opacity is important because it may show lung fibrosis and requires long-term follow-up. Air trapping is also important because it shows obstruction of small bronchioles and is probably a radiographic sign of bronchiolitis obliterans.

We found local fibrosis in about 8% of patients, which was similar to the studies of Emad et al. and Hafezi et al. (5, 15).

In most cases, lower lung lobes were most frequently affected, which is probably due to the fact that lower lobes are larger than upper lobes.

CONCLUSION

We found a high frequency of HRCT abnormalities among mustard gas-exposed veterans, and most abnormalities were irreversible. Therefore, we recommend that periodic pulmonary assessments be performed for these patients. In our study, HRCT findings included diffuse hyper-aeration, interstitial opacity, parenchymal opacity, bronchiectasis, sub-pleural air trapping, and local fibrosis. Other areas that warrant further study in terms of patient exposure to mustard gas include the cellular effects of mustard gas and genetic markers indicating exposure to mustard gas.

ACKNOWLEDGMENTS (FUNDING SOURCES)

We would like to thank all study participants. This study was funded by Shahid Sadoughi University of Medical Sciences.

AUTHER CONTRIBUTIONS

All authors contributed equally in this study.

CONFLICT OF INTEREST

There are no conflict of intrest.

ETHICAL STANDARDS

Informed consent was obtained from each participant. This study was approved by the ethics committee of Shahid Sadoughi University of Medical Sciences (number 1017).

REFERENCES

1. Bullman T, Kang H. A fifty year mortality follow-up study of veterans exposed to low level chemical warfare agent, mustard gas. Annals of epidemiology. 2000;10(5):333-8.
2. Franz DR, Jahrling PB, Friedlander AM, McClain DJ, Hoover DL, Bryne WR, et al. Clinical recognition and management of patients exposed to biological warfare agents. The Journal of the American Medical Association. 1997;278(5):399-411.
3. Razavi SM, Ghanei M, Salamati P, Safiabadi M. Long-term effects of mustard gas on respiratory system of Iranian veterans after Iraq-Iran war: a review. Chinese Journal of Traumatology. 2013;16(3):163-8.
4. Khateri S, Ghanei M, Keshavarz S, Soroush M, Haines D. Incidence of lung, eye, and skin lesions as late complications in 34,000 Iranians with wartime exposure to mustard agent. Journal of occupational and environmental medicine. 2003;45(11):1136-43.
5. Hefazi M, Attaran D, Mahmoudi M, Balali-Mood M. Late respiratory complications of mustard gas poisoning in Iranian veterans. Inhalation toxicology. 2005;17(11):587-92.
6. Hassan ZM, Ebtekar M, Ghanei M, Taghikhani M, Daloii MRN, Ghazanfari T. Immunobiological consequences of sulfur mustard contamination. Iranian Journal of Allergy, Asthma and Immunology. 2006;5(3):101-8.

7. Dacre JC, Goldman M. Toxicology and pharmacology of the chemical warfare agent sulfur mustard. Pharmacological reviews. 1996;48(2):289-326.
8. Balali-Mood M, Hefazi M. The pharmacology, toxicology, and medical treatment of sulphur mustard poisoning. Fundamental & clinical pharmacology. 2005;19(3):297-315.
9. Bakhtavar K, Sedighi N, Moradi Z. Inspiratory and expiratory high-resolution computed tomography (HRCT) in patients with chemical warfare agents exposure. Inhalation toxicology. 2008;20(5):507-11.
10. Wada S, Miyanishi M, Nishimoto Y, Kambe S, Miller R. Mustard gas as a cause of respiratory neoplasia in man. The Lancet. 1968;291(7553):1161-3.
11. Austin J, Müller N, Friedman PJ, Hansell DM, Naidich DP, Remy-Jardin M, et al. Glossary of terms for CT of the lungs: recommendations of the Nomenclature Committee of the Fleischner Society. Radiology. 1996;200(2):327-31.
12. Ghanei M, Fathi H, Mohammad MM, Aslani J, Nematizadeh F. Long-term respiratory disorders of claimers with subclinical exposure to chemical warfare agents. Inhalation toxicology. 2004;16(8):491-5.
13. Bagheri M, Hosseini S, Mostafavi S, Alavi S. HIGH-Resolution CT in chronic pulmonary changes after mustard gas exposure. Acta Radiologica. 2003;44(3):241-5.
14. Ghanei M, Mokhtari M, Mohammad MM, Aslani J. Bronchiolitis obliterans following exposure to sulfur mustard: chest high resolution computed tomography. European journal of radiology. 2004;52(2):164-9.
15. Emad A, Rezaian GR. The diversity of the effects of sulfur mustard gas inhalation on respiratory system 10 years after a single, heavy exposure: analysis of 197 cases. CHEST Journal. 1997;112(3):734-8.
16. Bijani K, Moghadamnia A. Long-term effects of chemical weapons on respiratory tract in Iraq–Iran war victims living in Babol (North of Iran). Ecotoxicology and environmental safety. 2002;53(3):422-4.
17. Biederer J, Schnabel A, Muhle C, Gross W, Heller M, Reuter M. Correlation between HRCT findings, pulmonary function tests and bronchoalveolar lavage cytology in interstitial lung disease associated with rheumatoid arthritis. European radiology. 2004;14(2):272-80.